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UNDER THE EDITORIAL DIRECTION OF
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No. 1

Original Communications

INVESTIGATION OF THE PATENCY OF PERIPHERAL ARTERIES*

P. FORMIJNE, M.D.
AMSTERDAM, HOLLAND

ARTERIAL PALPATION

ONE of the most important methods for the study of peripheral vascular diseases is the palpation of the arteries of the extremities.† In the arm the brachial, radial and ulnar arteries are easily palpable; in the leg the femoral, posterior tibial, and dorsal pedal arteries usually can be palpated without difficulty. The palpation of the popliteal artery is more difficult; pulsations may not be felt in this artery even when the arteries of the feet show normal pulsations. It is a widely accepted opinion that absence of pulsation in these arteries does not occur in normal individuals, or at least occurs very rarely. This opinion is not wholly justified by a study of the literature. Only a small number of investigations has been published, and there is no agreement on this important question.

Erb investigated clinically 381 persons without manifest arterial disease. He found absence of pulsation in both the posterior tibial arteries in 2 cases; absence of pulsations in the posterior tibial and dorsalis pedis arteries of one foot in two cases. Absence of pulsation in one or more arteries of the feet was therefore found only in 1 per cent of the control cases. Goldflamm investigated 200 persons, but not clinically. He found absence of pulsation in the arteries of the feet in 5 per cent of his cases. Buerger found in 200 persons normal pulsation in the dorsal pedal arteries in all but one case (0.5 per cent); the condition of the posterior tibial arteries is not mentioned in this series.

The agreement between these authors is satisfactory. The results

*From the Internal Clinic, University of Amsterdam, Wilhelminagasthuis.

†The expression "palpation of arteries" is used hereafter instead of the more correct expression "palpation of the pulsations in arteries."

obtained by Schneyer showed a fundamental difference. A clinical investigation of 500 persons showed absence of pulsation in males in 17 per cent; in females in 29 per cent. It is difficult to give an explanation of this divergence of results. It may be dependent upon differences in the ability to palpate still existing after a long experience with this method.

It is highly desirable to have this problem elucidated by the cooperation of many investigators. The need of an objective method for the control of the palpation is hereby emphasized. The scope of the present investigation was the study of this problem.

OSCILLATIONS

When blood pressure is measured with the instrument of Riva Rocci, oscillations are visible between systolic and diastolic pressure. These

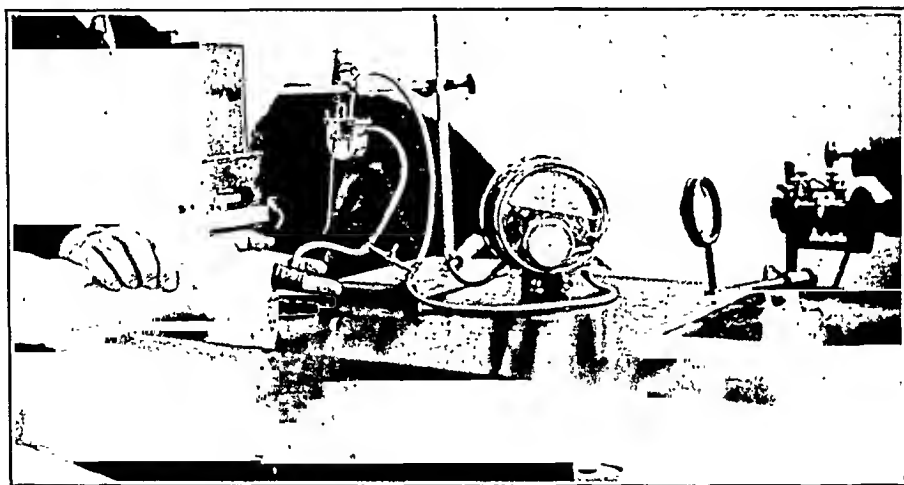


Fig. 1.—Photographic registration of oscillations of the left middle finger with a capsule of Gaertner (see Fig. 2). The oscillograph is suspended in the light beam of a Cambridge electrocardiograph. The capsule is inflated at a pressure of 70 mm. of mercury with the instrument of Pachon.

oscillations can be studied visually, or registered with an oscillograph on smoked paper or a photographic film. In the present investigation an oscillograph of Boulitte, suspended in the light beam of an electrocardiograph, was used (Fig. 1).

It was found necessary to obtain the oscillations of the most distal parts of the extremities. The dorsum of the foot was covered with a small cuff which was fastened around the foot with leather straps. When the cuff was connected with the oscillograph, distinct oscillations appeared.

It was soon apparent that these oscillations were not exclusively from the dorsum of the foot, but also in a small measure from the plantar side. Evidently the systolic expansion was transmitted by the leather

straps to the cuff. When the cuff was fastened on the plantar side again, the oscillations were predominantly but not exclusively from this side. On the hands no good results were obtained with this small cuff. After trying different methods the best results were given by the capsules of Gaertner (Fig. 2). They consist of a hollow metal cone, which is covered with a loose rubber membrane on the inside. This is fastened at the borders of the cone. On one place the cone is pierced and connected with a small metal tube. When the capsule is applied around the finger and the cuff inflated through the metal tube, the space between cone and membrane is filled with air and the membrane is pressed against the finger. If the capsule is connected with the oscillograph, small os-

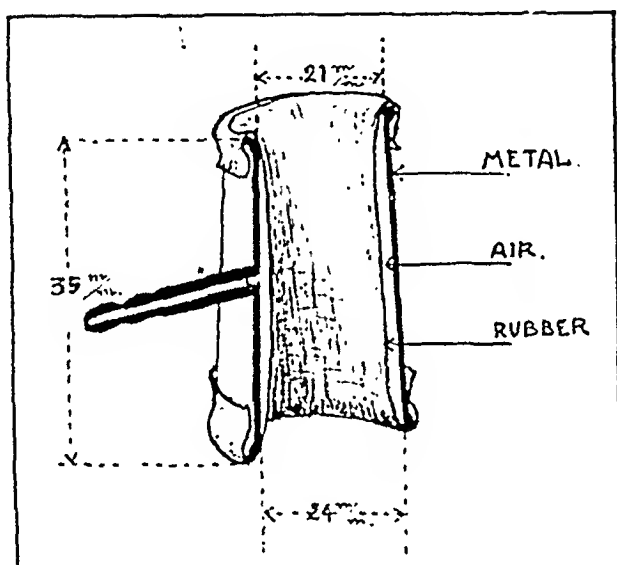


Fig. 2.—Section through capsule of Gaertner. The measurements are those of a commonly used model. Capsules of different sizes are used, according to the diameter of the finger.

illations from the fingers can be registered. In the same manner oscillations from the arteries of the big toes can be taken with an oval cone.

DETERMINATION OF THE SO-CALLED OCCULT BLOOD PRESSURE BY THE METHOD OF GAERTNER

The capsules of Gaertner, as described above, were originally used for the determination of the blood pressure in a finger. The finger was made anemic by pushing a narrow rubber ring from the end of the finger to the base. Then the capsule was placed over the middle phalanx and inflated above systolic pressure. After the rubber ring was cut, the blood filled the finger up to the capsule. Then the pressure in the capsule was diminished slowly. At a certain pressure there was a sudden filling of the finger tip with blood. At this instant the blood

pressure in the finger was just able to overcome the pressure in the capsule. This pressure was assumed to be the systolic pressure in the finger (Fig. 3).

This method is no longer used for its original purpose, that of determination of the general blood pressure. Changes in the condition of the finger arteries do not allow constant results. Nevertheless this

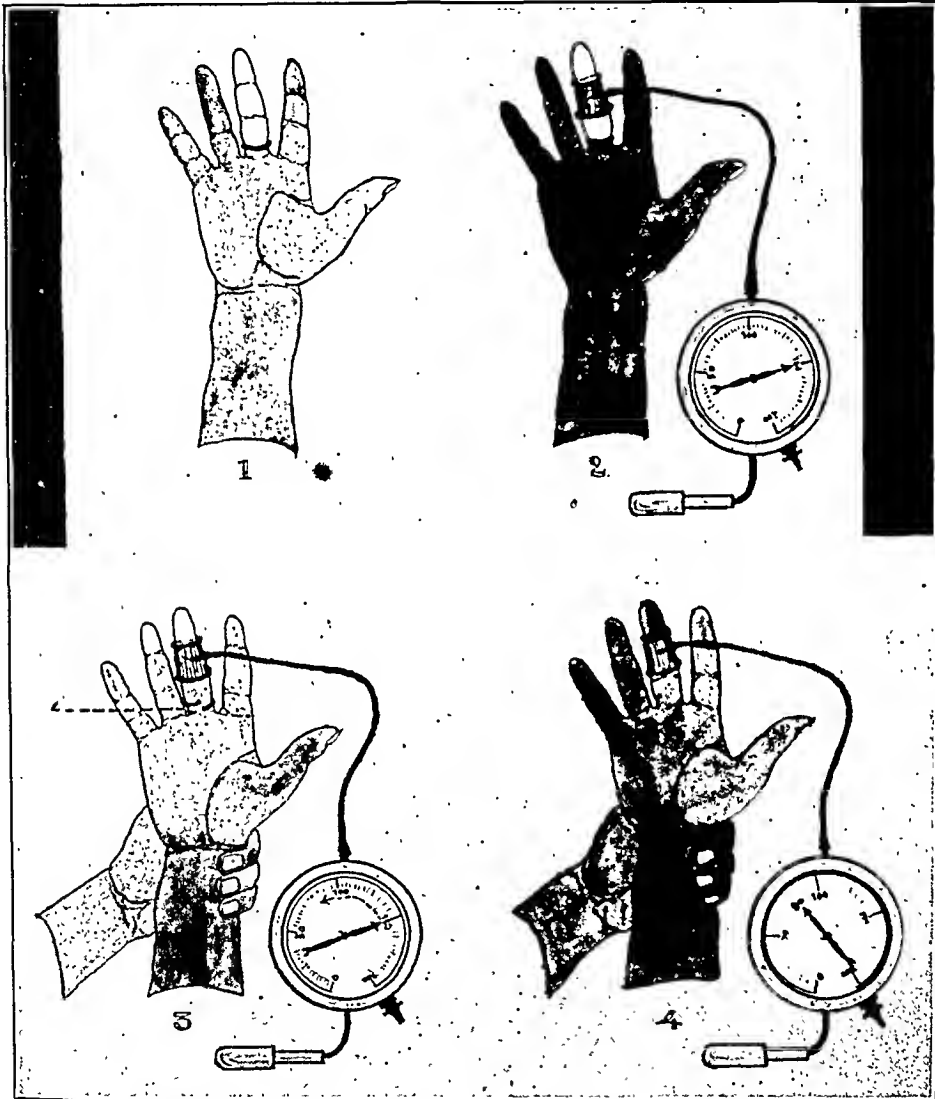


Fig. 3.—Determination of occult blood-pressure with the method of Gaertner.
 First phase: A rubber ring is pushed over the third right finger from the end to the base.
 Second phase: A capsule of Gaertner, connected with a manometer is placed over the middle phalanx and inflated to a pressure of 150 mm. of mercury.
 Third phase: The rubber ring is cut. After this the pressure is diminished slowly.
 Fourth phase: At a pressure of 80 mm. of mercury there is a sudden filling of the finger with blood.

method, in the procedure called determination of occult blood pressure, is very useful in the study of arterial diseases. It is the only practical method of blood pressure determination independent of the pulsatory phenomena.

It is quite possible, under certain circumstances that the change from a pulsating blood stream to a continuous stream does not take place, as is usually the case, in the arterioles and capillaries, but in the main arteries.

This possibility was first clearly formulated by L. Bard; he found in a patient with stenosis of the subclavian artery no pulsations on the left side, while the fingers showed a normal occult blood pressure. He assumed that the stenosis of the subclavian artery had abolished the oscillations, without changing the blood pressure. This combination must be considered a rare one. The occurrence of a continuous blood stream is often seen in some diseases, especially arterial embolism, but in most cases there is very marked lowering of the occult pressure.

The occult blood pressure also can be determined at higher levels (ankle, wrist, etc.). In this case the extremity is made anemic by elevation and application of a rubber bandage. The cuff is then fastened around the limb at the level of determination, and inflated above systolic pressure. The bandage is removed, the limb placed horizontally, and the pressure in the cuff is gradually diminished until filling of the distal parts is to be seen. It is not always possible to make an accurate determination, especially in patients with slow circulation, or with irregularities of the pulse (for instance auricular fibrillation). In these cases only approximative values can be obtained.

COMPRESSION METHOD

Normal persons always showed oscillations in most fingers. Sometimes the oscillations were very small or absent in one finger (usually the fifth). These oscillations are derived from the main arteries of the hand, especially the radial and the ulnar artery. The relative significance of these arteries can be found by alternative compression of each of them.

When one of these arteries is closed by an obstructive arterial disease, compression of the other artery will abolish the oscillations in all fingers.

The principle of this method was first used by Allen: When the fist is clenched and the radial artery compressed, there is no filling on opening the hand when the ulnar artery is closed. Only an approximation can be given by this method.

The results of arterial compression can be demonstrated most conveniently in some patients with unilateral arterial obstruction.

CASE 1.—W. S., a man aged forty years, visited the clinic because of whiteness and pain in the fingers. Arterial palpation demonstrated absence of pulsation of the right ulnar and left dorsal pedal artery. Hereupon the arteries were studied with the compression method. The oscillations of every finger were registered under a pres-

sure of 60 mm. of mercury. First the radial artery was compressed; after that the ulnar artery. At last radial and ulnar arteries were both compressed at the same time (Fig. 4).

On the left hand there was no marked change in the oscillations when either the radial or the ulnar artery was closed. During compression of both arteries the oscillations disappeared entirely in all fingers.

On the right hand there was complete disappearance of the oscillations in all

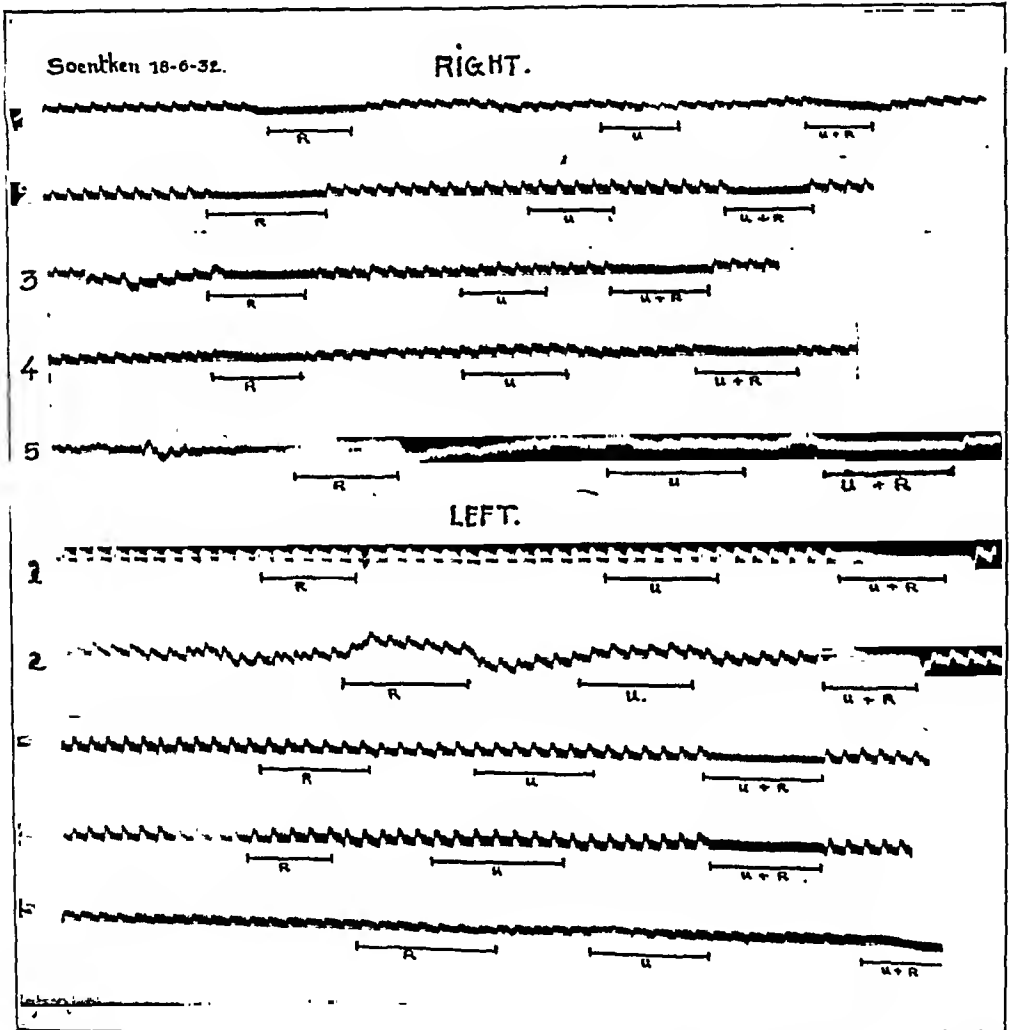


Fig. 4.—Case 1. June 18, 1932. Compression curves of all fingers of the right and left hand.

R = Period of compression of the radial artery.

U = Period of compression of the ulnar artery.

U + R = Period of compression of the ulnar artery and radial artery.

Compression of the radial artery causes a complete disappearance of oscillations in all fingers of the right hand. Occlusion of the right ulnar artery is demonstrated.

fingers when the radial artery alone was compressed. Compression of the ulnar artery had no effect. The conclusion was that at this pressure the oscillations of the fingers came only from the radial artery.

It is possible that oscillations coming from the ulnar artery were present at lower pressures in the capsule. This possibility could be excluded by compression of the radial artery at different pressures (from 80 mm. to 10 mm. of mercury). Always

there was complete disappearance of oscillations when the radial artery was closed. Finally the existence of a continuous blood stream through the ulnar artery was

TABLE I

	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. RADIAL ART.	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. ULNAR ART.
R. second finger	40 70*	0	80	75
R. fourth finger	85	0	95	90
L. second finger	30	65	60	40
L. fourth finger	90	100	100	90
	SPONT. OCCULT PRESSURE			
R. second finger				
R. fourth finger				
L. second finger	60			
L. fourth finger	100			

*Value after repetition of the determination (see text).

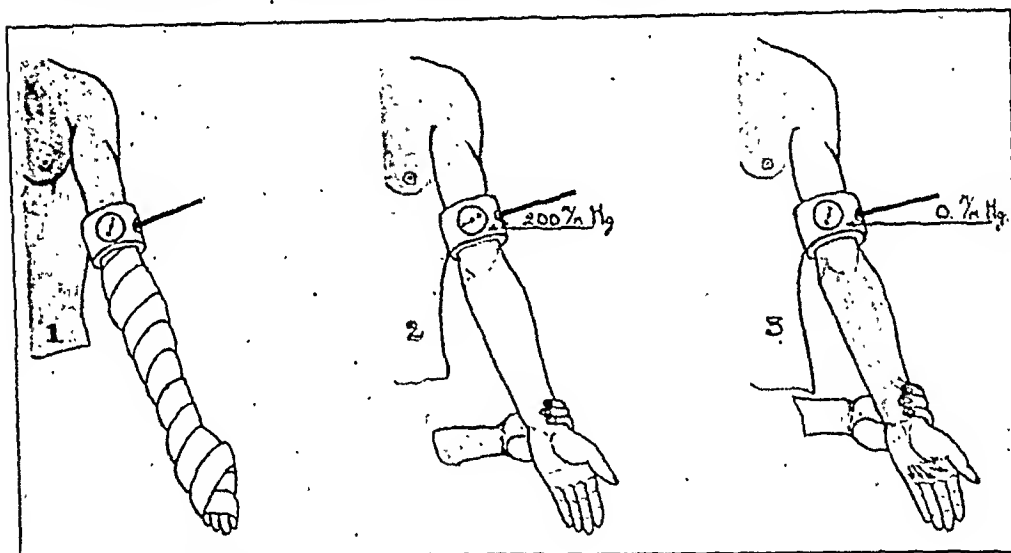


Fig. 5.—Shock method.

First phase: The arm is made anemic with a rubber bandage.

Second phase: A cuff is applied over the upper arm and inflated to a pressure of 200 mm. of mercury. The rubber bandage is taken off.

Third phase: The cuff is suddenly deflated during compression of the radial artery. The blood streams in the lower arm and through the ulnar artery slowly in the hand. The ulnar artery is patent to some degree.

considered. For this investigation the influence of the arterial compression on the occult blood pressure was determined as described above. Before and after every determination with arterial compression the spontaneous occult pressure was determined to avoid errors by variations in the pressure during the investigation. The results obtained in the second and fourth fingers of both hands are given in Table I.

Table I shows that in the left hand compression of one artery (radial or ulnar) caused no, or only a small, lowering of the occult blood pressure. The low value that was found in the first determination in the left and right second finger probably was caused by a contraction of the finger arteries (this very low value for the occult pressure in the first determination was seen also in other cases). On the right hand, compression of the radial artery caused a fall of the occult pressure to zero! So it was proved that the blood stream in the fingers of this hand came almost totally from the radial artery. But with another method, which subsequently is called shock

method, there could be demonstrated a slight permeability of the ulnar artery (Fig. 5). The arm was made anemic by elevation and bandaging, and the circulation was cut off by inflation of a cuff around the upper arm. If the circulation was suddenly released, there was a sudden filling of the right and left arm and hands. When this experiment was repeated with the radial artery compressed, there was a fast filling of the hand on the left side through the open ulnar artery. On the right side there was a sudden filling of the lower arm up to the wrist. In the hand there was a very slow but progressive redness on the ulnar side and gradual filling of the hand and the finger. When the same experiment was repeated during compression of both the radial and the ulnar artery, there was no filling of the hand at the right or left side.

From these experiments the conclusion was drawn that there was still some degree of patency of the ulnar artery.

In the same manner the feet of this patient were investigated, and an almost total occlusion of the left dorsal pedal artery could be demonstrated.

A diagnosis of incipient thrombo-angiitis obliterans was made.

CASE 2.—A. R., a man aged fifty-three years, entered the ward with a diagnosis of luetic aortitis. During physical examination it was found that the left radial artery showed only very small pulsations, while the right radial artery pulsated normally. The pulsations of the left ulnar artery were somewhat smaller than the pulsations of the right. The arterial tension on the left upper arm was 90-55, on the right upper arm 110-55. This small difference did not explain the pulsus differens. The compression method was used for distinguishing between a real pulsus differens and a pseudo pulsus differens, caused by a local lesion of the radial artery (Fig. 6). It was found that the oscillations of every finger on the right side came from both the radial and the ulnar artery. On the left side the oscillations disappeared completely during compression of the ulnar artery. Compression of the radial artery had no effect. This investigation was repeated three times, always with the same results.

The small pulsations that were felt in the left radial artery did not reach the fingers.

The determination of the occult blood pressure gave the results shown in Table II.

TABLE II

	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. RADIAL ART.	OCCULT PRESS. DURING COMPR. ULNAR ART.	SPONT. OCCULT PRESSURE
Right second finger	50	30	50	60
Right fourth finger		40	45	65
Left second finger	60	65	0	65
Left fourth finger	65	55	0	70

These results showed that the occult blood pressure on the right side depended upon the radial and the ulnar arteries, while on the left side no occult pressure dependent upon the radial artery was found.

With the shock method it was found that the filling of the hand during compression of the ulnar artery was rather prompt, although slower than on the right side. During compression of both the radial and the ulnar artery on the left side

there still was a rather prompt filling of the hand. It was clear that another artery was responsible for this filling. On the dorsum of the hand a small pulsating vessel was found. Compression of this extra artery together with the radial and ulnar arteries did not prevent filling of the hand, although it was much slower. This indicated the presence of a fourth artery participating in the filling of the hand; this artery could not be localized by palpation of the hand. Patency of the radial artery was not proved or disproved by these experiments.

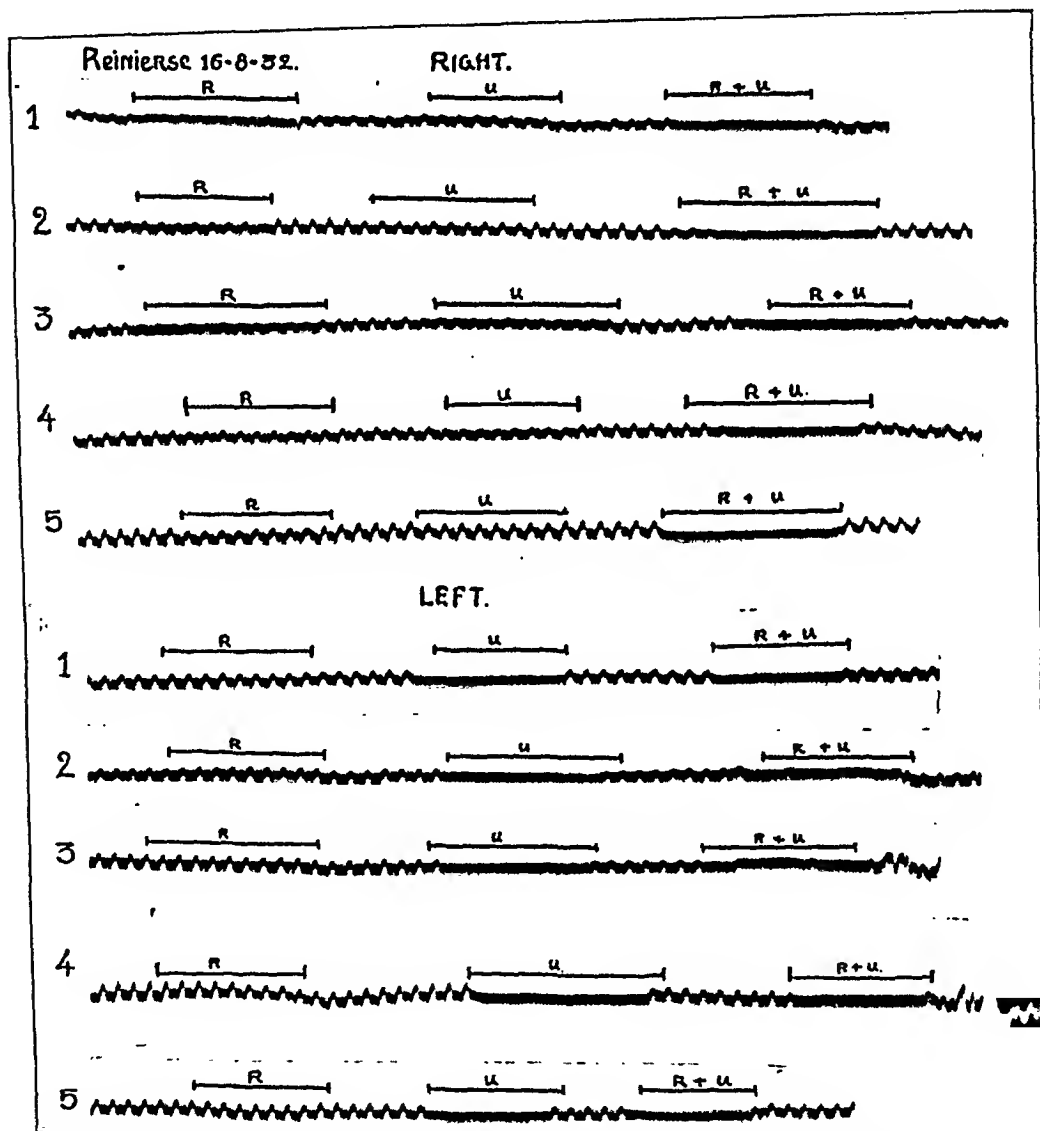


Fig. 6.—Case 2. August 16, 1932. Compression curves of all the fingers from the right and left hand. Compression of the ulnar artery causes a complete disappearance of the oscillations in all the fingers of the left hand. Occlusion of the left radial artery is demonstrated.

On the right side, compression of both the radial and the ulnar arteries prevented filling of the hand. Therefore no extra arteries could be demonstrated here. The normal interosseous artery seemed never to cause a filling of the hand.

The extra arteries on the left side were supposed to be collateral arteries, widened by the occlusion of the radial artery. This occlusion was only partial at the wrist (presence of small pulsation), but a total, or almost total, occlusion must have been present in a more distal part of the artery.

The conclusion was reached that this patient had a pseudo pulsus differens, caused by a local narrowing of the radial artery. The small difference in blood pressure between the right and left upper arms probably had no clinical significance.

The results obtained from examination of the two patients above show a strict agreement between both the compression curves of oscillations and the determinations of occult blood pressure during compression. Sometimes other results were obtained.

CASE 3.—Patient D. J., a man aged forty-seven years, with carcinoma of the stomach, was found to have a very small radial artery on the right side. The right ulnar artery was more developed than the left. Compression curves showed that on the normal left side the oscillations came from both the radial and the ulnar arteries. On the right side the oscillations came exclusively from the ulnar artery (with the exception of very faint oscillations in the right thumb, originating from the radial artery). Determinations of the occult blood pressure were made. (Table III.)

TABLE III

	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. ULNAR ART.	OCCULT PRESS. DURING COMPR. RADIAL ART.	DITTO
Right second finger	75	40	I 55	II 70
Left second finger	70	55	I 70	II 80
		OCCULT PRESS. DURING COMPR. ULNAR ART.	SPONT. OCCULT PRESSURE	
Right second finger		40	70	

Although the oscillations were of totally different composition on the right and the left side, there were no marked differences in the occult pressure.

This case presents an example of absence of pulsation with only slightly lowered occult pressure (right second finger during compression of ulnar artery). This combination was found to be rare.

CASE 4.—Miss V. C., thirty-eight years of age, had been visiting the clinic off and on for several years. She had marked arterial spasm of the Raynaud type in hands and feet; later she developed an extensive scleroderma on the chest and hips.

Arterial palpation showed absence of pulsations in the left dorsal pedal artery. The other arteries of feet and hands showed normal pulsation.

Arterial occlusion is not found in most cases of Raynaud's disease. The patency of the left dorsal pedal artery in this case with the typical clinical picture of Raynaud's was therefore investigated. (Fig. 7.)

Compression curves showed that the oscillations of the normal right foot came from both the posterior tibial and the dorsal pedal artery, with some preponderance of the latter. On the left foot the oscillations came exclusively from the posterior tibial artery.

These curves showed, in agreement with the arterial palpation, that the left dorsal pedal artery was not patent for oscillations. With a capsule especially fitted for the big toe the occult pressure was determined with the same technique as that described for the finger. Owing to technical difficulties the results were not so accurate as those on the finger, but nevertheless quite significant. (Table IV.)

TABLE IV

	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. A. TIB. POST.	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. A. DORS. PED.
Right big toe	75	95	90	60
Left big toe	70	0	110	90

	SPONT. OCCULT PRESSURE	OCCULT PRESS. DURING COMPR. A. TIB. POST.	OCCULT PRESS. DURING COMPR. A. TIB. POST. + A. DORS. PED.	SPONT. OCCULT PRESSURE
Right big toe	80	85	0	85
Left big toe	95	0		75

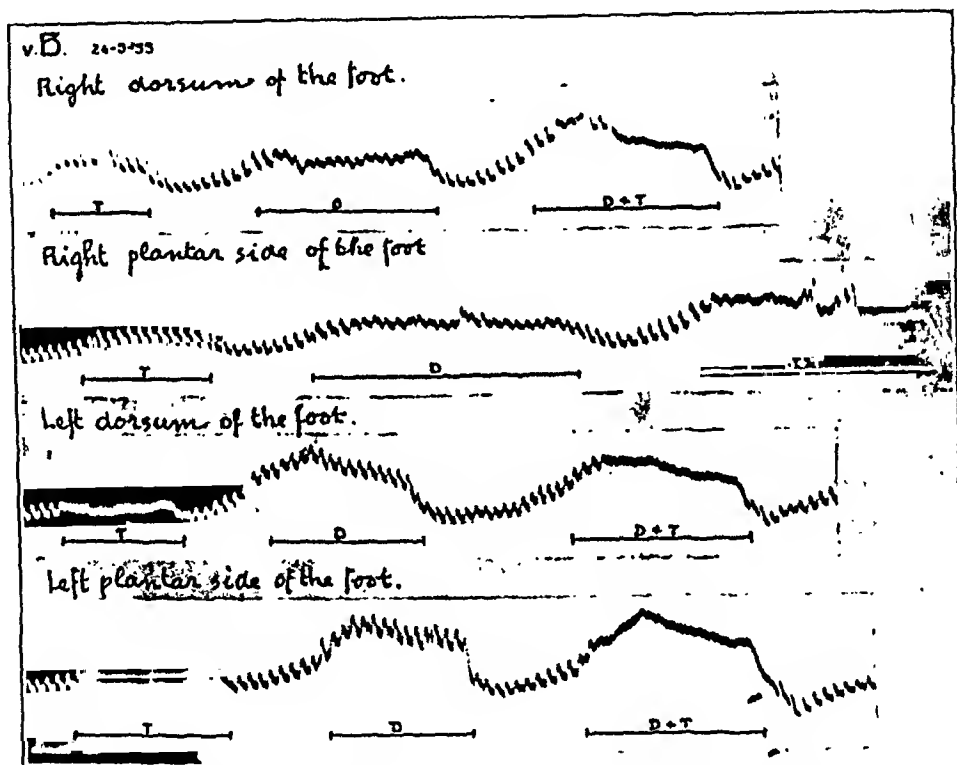


Fig. 7.—Case 4. March 24, 1933. Compression curves of the right and left foot.
 T = Period of compression of posterior tibial artery.
 D = Period of compression of dorsal pedal artery.
 T + D = Period of compression of posterior tibial and dorsal pedal artery.
 Compression of the posterior tibial artery causes complete disappearance of the oscillations in the left foot. Occlusion of the left dorsal pedal artery is demonstrated.

These results showed that compression of the posterior tibial artery had no effect on the normal right side, but gave a fall of the occult pressure to zero on the left side. Compression of the dorsal pedal artery had no effect on the left side, slight effect on the right side. An almost total occlusion of the left dorsal pedal artery had to be assumed. Now the shock method was carried out. The leg was made anemie, and arterial circulation was obstructed by a cuff, inflated to 220 mm. of mercury around the upper leg. Afterward the tension in the cuff was suddenly released, during compression of the posterior tibial artery. On the right side there was a prompt filling of the leg and the foot while the toes showed an irregular filling (arterial spasm). On the left side there was a prompt filling of the leg to the ankle. From this point there was a very slow progressive redness of the dorsum

of the foot, which, after two minutes had elapsed, had not yet reached the distal parts. Release of the posterior tibial artery gave a prompt filling of the foot. In this manner a very small degree of patency could be demonstrated in this artery.

The value of the methods described for the clinical investigation of arterial occlusion was proved on different groups of patients.

Compression curves of the hands.

1. In patients with normally pulsating radial and ulnar arteries. In this group curves were made of 24 patients. Arterial compression in these control cases showed some normal variations. Two extreme groups with many intermediate cases could be distinguished. In the first group compression of one artery alone (radial or ulnar) had no marked influence on the oscillations. Here it was evident that in all fingers the oscillations came from both arteries. When one artery was compressed, the other could compensate for the resulting loss of circulation.

In the second group there were differences between the fingers. The oscillation of the thumb and sometimes also of the second finger came only from the radial artery. In the third, fourth, and fifth fingers the influence of the ulnar artery gradually increased. Sometimes the fifth finger showed again a preponderance of the radial artery, especially when compared with the fourth finger.

2. Patients with absence of pulsations in one or both ulnar arteries. In this group 8 cases were investigated. One of these (Case 1) has been described above.

Table V shows that oscillations from the ulnar artery often could be demonstrated in cases which had no palpable pulsations of this artery.

In a case with changes in the patency of the ulnar arteries (No. 8 of Table V) compression curves gave a better insight into the condition of the artery than did arterial palpation. In the first two cases there was complete agreement between arterial palpation and compression curves. The determination of the occult pressure showed also an almost total occlusion. Compression of the radial artery caused a fall in pressure to zero (in both hands of the second case and in the right hand of the first case of the table).

In the other cases the relation between arterial palpation and compression curves was variable.

Determination of occult pressure showed in those cases that were investigated (Nos. 3, 5, and 8) that either the radial or the ulnar artery alone could uphold a good occult pressure in the fingers.

Compression curves of the arteries of the foot.

The influence of alternative compression of the posterior tibial and the dorsal pedal artery on the oscillations of the dorsal and plantar side of the foot was investigated in some groups of patients.

TABLE V

	NAME	AGE	DIAGNOSIS	NONPALPABLE ULNAR A.	RESULTANT COMPRESSION CURVES	
					OSC. R. HAND	OSC. L. HAND
1	W. T.	41 years	Thoracic aneurysm	Right	Exclusively from radial A.	Osc. mixed from radial A. and ulnar A.
2	A. K.	72 years	Tabes dorsalis	Both	Exclusively from radial A.	Exclusively from radial A.
3	N. d. G.	32 years	Auricular fibrillation	Both	Exclusively from radial A.	Almost exclusively from radial A.
4	L. F.	47 years	Scleroderma	Both	Exclusively from radial A.	A. (except faint osc. thumb) Almost exclusively from radial A. A. (except faint osc. third and fourth fingers)
5	D. S.	53 years	Sprue	Both	Almost exclusively from radial A. (except faint osc. first, fourth, fifth fingers)	Mixed from radial and ulnar A.
6	H. B.	50 years	Auricular fibrillation	Right	Mixed from radial and ulnar A.	Mixed from radial and ulnar A.
7	C. M.	51 years	Cardiac asthma	Right	Mixed from radial and ulnar A.	Mixed from radial and ulnar A.
8	10/8 C. B.	64 years	Pernicious anemia	Both	Almost exclusively from radial A. (except faint osc. first and fourth fingers)	Mixed from radial and ulnar A.
5/9				Right	Predominant from radial A. (however, distinct osc. from ulnar A. in all fingers)	Mixed from radial and ulnar A.
6/9	Fever (temp. 38.4°)			Neither	Predominant from radial A. (however, distinct osc. from ulnar A. in all fingers)	Mixed from radial and ulnar A.
20/9				Right	Predominant from radial A. (however, distinct osc. from ulnar A. in all fingers)	Mixed from radial and ulnar A.

Control group.

1. Patients with normal pulsations in the posterior tibial and the dorsal pedal artery	30 cases
Oscillations from both arteries present	27 cases
Oscillations from only one artery present	3 cases

These three cases need a special discussion. In one case the oscillations were too small and indistinct to make the forming of a reliable judgment possible. The second case had a peculiar arterial disease, which was diagnosed as thrombo-angiitis obliterans of the (digital) arteries of the toes. In this case the oscillations in both feet came from the posterior tibial arteries only, although there were normal pulsations in the dorsal pedal arteries. A possible explanation was an obliteration of the principal branches of the dorsal pedal artery. In a third case, with Addison's disease, there were small but distinct oscillations, which came only from the dorsal pedal arteries. The posterior tibial arteries showed normal pulsations. Why these pulsations could not be demonstrated on the foot was not explained.

These results showed that in most cases with normally pulsating arteries of the feet there were on the dorsal and plantar side oscillations from both arteries; exceptionally the oscillations came only from one artery.

2. Patients with absence of pulsations in one or both dorsal pedal arteries.

<i>Absence of pulsations in both dorsal pedal arteries</i>	9 cases
Oscill. <i>only</i> from post. tib. art. in both feet	6 cases
Oscill. <i>only</i> from post. tib. art. in one foot and predominantly from post. tib. art. in the other foot (with faint oscill. from the dorsal ped. art.)	2 cases
Oscill. from both the post. tib. and dors. ped. art.	1 case
<i>Absence of pulsations in one dorsal pedal artery</i>	4 cases
Oscill. <i>only</i> from the post. tib. art. of the same side	3 cases
Oscill. from both the post. tib. and the dors. ped. arteries of the same side	1 case

In nine cases of this group there was strict agreement between pulsations and oscillations. In two cases there was a very slight difference. In two cases there was no agreement. In these latter cases patency of dorsal pedal arteries that showed no pulsation on palpation was proved.

3. Patients with absence of pulsations in one or both posterior tibial arteries.

<i>Absence of pulsations in both post. tib. arteries</i>	6 cases
Oseill. in both feet from the dors. ped. art. only	2 cases
Oseill. in both feet from both the post. tib. and the dors. ped. art.	4 cases
<i>Absence of pulsations in one post. tib. artery</i>	2 cases
Oseill. on the same side from the dors. ped. art. only	1 case
Oseill. on the same side from both the post. tib. and the dors. ped. art.	1 case

In this group there was strict agreement between pulsations and oscillations in 3 out of 8 cases. In the other cases patency of the posterior tibial arteries had to be assumed, although pulsations could not be felt. Absence of patency for oscillations in the posterior tibial artery seems to be rare in patients without manifest arterial disease.

The following conclusions could be drawn:

1. When no pulsations of the dorsal pedal artery were felt, there were no oscillations from this artery in most cases.
2. When no oscillations from the dorsal pedal artery were found, there were no pulsations in this artery in most cases.
3. When no pulsations were found in the *posterior tibial artery*, often oscillations from this artery could be detected.

These results indicated that the palpation of the posterior tibial artery is less reliable than palpation of the dorsal pedal artery.

The compression method can demonstrate the patency of arteries irrespective of palpation. It cannot prove with absolute certainty the occlusion of arteries. It should therefore be combined with the determination of occult blood pressure and the shock method. The degree of patency of the arteries of the extremities can be estimated with a fair degree of accuracy by the combination of these methods.

SUMMARY

1. A method for the registration of arterial oscillations in fingers and feet is described.
2. This method is used as a test for the patency of the main arteries. By alternative compression of the radial and ulnar arteries on the hand, of the posterior tibial and dorsal pedal arteries on the feet, the composition of the oscillations can be studied.
3. The so-called occult blood pressure in fingers and big toes was studied by the method of Gaertner. The influence of compression of arteries on the occult blood pressure was studied and used for testing the patency of these arteries.
4. A third method, called shock method, was used for testing the patency of almost totally occluded arteries. Most of these arteries were found to have some degree of patency.

5. The relation between the results of arterial palpation and the compression method was investigated in different groups of patients.

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TREATMENT OF CHRONIC HEART DISEASE BY TOTAL ABLATION OF THE THYROID GLAND*†

VII. THE HEART IN ARTIFICIAL MYXEDEMA

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STUDIES of the heart in spontaneous myxedema^{3, 10, 21, 26, 28, 30, 34} during the past decade have demonstrated that (1) the heart size, as measured by the seven-foot roentgenogram, is increased; (2) the voltages of the P, T, and QRS waves of the electrocardiogram are frequently diminished;^{15, 31, 33, 35, 36} and (3) cardiac contractions are less vigorous.^{2, 30} Opinions differ concerning the clinical significance of these alterations. Zondek^{42, 43} and Fahr¹⁴ maintain that cardiac function is often impaired in patients with myxedema having such changes. Christian,^{11, 12} Willins and Haines,⁴¹ Case,¹⁰ Means, White and Krantz,²⁸ however, studied a total of three hundred patients with myxedema and concluded that heart function is rarely, if ever, impaired. From a recent review of the literature and a comprehensive study of thirty additional cases at the Massachusetts General Hospital, Lerman, Clark and Means²¹ conclude that "myxedema heart" in the sense of heart failure occurs rarely, if at all. The studies of the above investigators were confined almost entirely to patients without cardiovascular disease.

In treating patients with chronic heart disease and other conditions by inducing hypothyroidism by total removal of the normal thyroid gland, we have been able to study the development of the cardiovascular changes associated with the development of myxedema. Two aspects of the heart in myxedema have been investigated: first, the character and rate of development of the changes in heart size and electrocardiographic tracings; and, second, the significance of these changes in terms of cardiac function. Studies before, and at varying intervals after, total thyroidectomy have been made in three groups of patients: one group comprising patients with congestive heart failure at the time of, or just before, operation; the second group, patients with angina pectoris; and the third group, patients with no evident functional or anatomical abnormalities. The rationale, technic, and therapeutic results of total thyroidectomy in patients with chronic heart disease and no thyrotoxicosis have been described in previous communications.^{4, 8, 9, 15, 16, 37}

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MATERIAL AND METHODS

Thirty-seven patients in whom total thyroidectomy was performed have been studied.* Clinical observations on some of these patients have been reported;⁹ observations on the others are to be reported later. The ages of the patients varied from fourteen to sixty-six years; twenty-three were males, and fourteen females. Twenty-two patients showed congestive failure at the time of, or prior to, operation; ten had angina pectoris without congestive failure; one had uncontrollable paroxysmal auricular fibrillation; and four had no cardiovascular disease, the operation having been performed for other reasons. A persistently low basal metabolic rate was obtained in every case after thyroidectomy.

The degree and progress of the hypothyroid state in the subjects of this investigation have been judged by the following indices: (1) basal metabolic rate; (2) velocity of blood flow; (3) serum cholesterol; and (4) clinical observations. Each of these measurements, together with blood pressures and heart rates, was obtained before and at appropriate intervals after thyroidectomy.

The data on the heart size and the electrocardiographic tracings have been analyzed in reference to the degree of hypothyroidism as evaluated on the basis of all these four factors. The postoperative period of study varied in the different patients from one and one-half to twelve months. The earliest postoperative observations on electrocardiographic tracings and heart size were made within the first month after operation.

Teleroentgenograms were taken in the standard manner at the height of inspiration; since appreciable change in the position of the diaphragm may produce apparent changes in heart size. Measurements of the internal diameter of the chest were made to evaluate approximately the position of the diaphragm in successive films. The three standard leads of a No. 2 Hindle electrocardiograph were used. Basal metabolic rate measurements were made in duplicate with a Collins-Benedict-Roth apparatus, and results calculated according to the Aub-DuBois normal standards.¹ The values reported are the average of duplicate analyses which checked within 5 per cent. The preoperative values represent the average of several such measurements on different days. Measurements preoperatively and during the first three to six postoperative weeks were made while the patient was in the hospital. When studied after discharge from the hospital, the patient rested quietly in bed from one-half to one hour before measurements were made. Serum cholesterol measurements were made in duplicate by the method of Myers and Wardell²⁹ using the continuous extraction apparatus described by Ling.²² Blood was drawn from the antecubital vein with minimal stasis, after a fast of fourteen hours or more. The arm-to-tongue circulation time, as measured by the decholin method of Winternitz, Deutsch and Brull⁴⁰ was used as an index of the velocity of blood flow. The heart rates were measured in the basal state. Blood pressure measurements were made by means of a standard mercury manometer with a cuff 14 cm. wide. The readings represent the mean values of repeated measurements made with the patient at rest. The above measurements and clinical observations at various time intervals were obtained on the same day or subsequent days.

FACTORS EMPLOYED IN GAUGING THE DEGREE OF HYPOTHYROIDISM

Although measurement of the basal metabolism is the most useful single estimation available for evaluating the degree of thyroid activity, the basal metabolic determinations fail at times to conform to those ex-

*All operations were performed by Dr. David D. Berlin.

peeted from clinical studies. For example, no clinical evidence of reduced thyroid activity may be manifest in certain patients whose basal metabolic rates are reduced as low as 25 or even 35 per cent below the average normal.²⁷ On the other hand, the administration of dinitro-orthoeresol or dinitrophenol^{13, 36} to patients with myxedema may increase the metabolic rate, with little or no influence on the clinical signs and symptoms of myxedema. The rise in metabolic rate after the administration of dinitrophenol or dinitro-orthoeresol to normal persons or to patients with myxedema is not accompanied by the nervous symptoms and cardiovascular manifestations which are subsequent to thyroid administration.^{13, 36} In the light of these facts, the metabolic rate must be considered merely one expression of the underlying hypothyroid state.

The importance of the serum cholesterol value as an aid in estimating the degree of spontaneous myxedema has been stressed by Hurxthal,^{19, 20, 23} and the findings in artificial myxedema will be described by us in a forthcoming communication.¹⁷ In some patients the height of the serum cholesterol was in closer agreement with the clinical signs and symptoms of hypothyroidism than the basal metabolic rate (Cases 5, 12, 15, 16).

The relation between the metabolic rate and velocity of blood flow in health and disease has been described in previous communications.^{5, 6, 7, 38} In patients with cardiovascular disease and a normal metabolic rate, the velocity of blood flow is slowed according to the degree of circulatory insufficiency. The blood flow may be similarly slowed in patients with no cardiac failure but with the low metabolic rates of myxedema. The velocity of blood flow in the latter patients is a further index of the degree of hypothyroidism.

The development of clinical signs and symptoms of hypothyroidism following operation usually indicated roughly the degree of the hypothyroid state. As the basal metabolic rate became significantly lowered following operation, mild signs and symptoms, such as dryness of the skin, slow growth of hair, slight hoarseness, and coldness of the extremities, appeared. The interval between operation and the development of these signs and symptoms and of a markedly reduced basal metabolic rate varied usually from three weeks to two months. These early symptoms caused little or no discomfort and did not require thyroid medication. As the basal metabolic level continued at or below approximately minus 30 per cent, many patients showed weakness of the legs, puffiness of the face and hands, drowsiness, and irritability. These "untoward symptoms" of myxedema were controlled by means of small doses of thyroid (Armour's), one-eighth to one-half grains daily.

TABLE I

RELATIONSHIP OF BASAL METABOLIC RATE, VELOCITY OF BLOOD FLOW AND BLOOD CHOLESTEROL TO CHANGES IN THE SEVEN-FOOT ROENTGENOGRAM OF THE HEART IN PATIENTS WITH CONGESTIVE FAILURE BEFORE AND AFTER TOTAL ANNIHILATION OF THE NORMAL THYROID GLAND

NO.	INIT. DIAG.	SEX	AGE	TIME INT.	TRANS. CARDIAC		LENGTH	BASE	HAUF CHEST DIAM.	B. M. R. PER CENT	VMP IN SEC. ONDS	CHOL. MG./100 C.C.	THYROID MEDICATION	BASAL PULSE	B. P. MM.
1.	L. B. R. H. D.	F	44	Pre-op. 1 mo. 2½ mo. 6 mo. 8½ mo.	13.9 13.6 13.9 15.4 16.6	14.2 14.1 14.8 15.8 16.7	11.2 11.0 11.3 11.0 11.1	11.0 11.1 10.9 11.1 11.1	-9 -32 -25 -37 -32	20 23	132	140/78 112/82 140/90 130/86 128/76		60 44 60 58 70	
2.	H. G. R. H. D.	M	22	Pre-op. 1½ mo. 3½ mo. 4½ mo. 5 mo.	15.3 16.9 17.2 17.7 16.9	17.0 17.9 18.1 17.7 17.3	12.7 14.0 14.2 14.4 12.8	14.5 14.9 14.8 14.9 14.4	+7 -28 -27 -22 -38	34 42 56 51 37	138 251 236	110/60 118/70 88 116/80 110/68	0.4 mg. thyroxin daily	80 70 88 70 66	
3.	E. W. R. H. D.	M	27	Pre-op. 1 mo. 3 mo. 6½ mo.	17.3 18.0 18.9 19.6	17.3 17.5 18.2 19.4	13.4 14.0 13.3 13.3	15.9 16.1 16.2 16.4	+5 -22 -27 -34	23 40 52 43	127 135 149 181	110/60 104/60 110/66 106/66		80 76 80 70	
4.	C. C. H. H. D. L. H. D.	M	66	Pre-op. 3 wk. 1 mo. 14 mo. 6½ mo.	15.8 16.3 18.0 16.8 16.7	18.5 18.0 19.3 19.2 18.2	13.0 11.8 11.2 12.7 13.2	14.8 14.8 14.5 15.0 15.0	+9 -23 -26 -23 -30	33 66 50 40 53	151 147 207 196 206	130/70 116/68 112/68 128/70 110/70	gr. 1½ daily gr. 1½ daily	47 45 50 65 58	
5.	S. Br. R. H. D.	F	47	Pre-op. 3½ mo.	17.8 19.7	18.0 20.0	11.7 14.5	13.4 13.6	+13 -4	24 81	161 364	198/110 148/90		72 56	

R. H. D.—Rheumatic heart disease
A. H. D.—Arteriosclerotic heart disease
H. H. D.—Hypertensive heart disease

L. H. D.—Luetite heart disease
A. P.—Angina pectoris
C. A.—Cardiac asthma

C. T.—Healed coronary thrombosis
R. A.—Bronchial asthma
C. P.—Cor pulmonale

TABLE I—CONT'D

6.	F. C. B. A. C. P.	M	35	Pre-op. 1 mo. 2 mo. 4½ mo. 6 mo. 8 mo.	15.1 15.6 14.9 15.9 15.8 17.0		13.6 13.5 13.6 13.5 13.6 13.7	- 4 -24 -32 -27 -26 -37	22 32 31 28 39 38	154 217 255 216	66 50 56 66 76 70	118/80 112/86 112/86 112/90 116/92 108/92
										gr. ½ daily		
7.	F. Z. R. H. D. C. A.	M	19	Pre-op. 3½ mo.	17.0 18.6	19.1 20.2	13.9 14.5	+ 1 -10	26 25	138 254	90 98	300/ 0 200/ 0
8.	S. Be. R. H. D.	F	51	Pre-op. 1 mo. 3 mo. 4 mo. 5 mo. 6 mo.	14.6 16.0 16.2 15.5 15.8	16.5 16.6 16.8 14.8 16.6	13.6 12.5 13.5 11.8 11.9	+ 4 -12 -17 -14 + 8 + 4	31 40 55 182 38	154 311 128 246 182	70 82 62 60 60 76	140/82 132/88 112/60 120/60 132/82 120/80
										gr. ¼ daily		
9.	H. G. H. H. D.	F	38	Pre-op. 2 mo. 3 mo.	14.6 16.0	14.8 15.4	8.7 9.8	- 8 -25 -36	29 38 42	292 345	41 56 45	220/98 200/98 186/100
										gr. 1 for 5 days		
10.	W. B. H. H. D. C. A. A. P.	M	55	Pre-op. 3 wk. 1½ mo. 6½ mo.	13.6 14.6 14.8 14.3	18.4	16.3	+ 9 -15 -24 -33	18 23 24 34	294 335 388 410	66 70 56 62	180/110 128/80 140/82 155/90
										gr. ⅓ daily—1 mo.		
11.	G. F. A. P. R. H. D. C. T.	M	52	Pre-op. 1 mo. 5 mo. 7 mo. 10 mo. 12 mo.	17.4 18.2 18.0 17.9 18.5 17.7		14.8 14.6 14.7 14.6 14.5 14.6	- 1 -23 -25 -26 -25 -26	45 48 41 40 40	130/80 102/70 63	70 50 58 60 70 63	130/80 102/70 63

TABLE 1 (CONT'D)

NO.	INIT. DIAG.	SEX	AGE	TIME INT.	TRANS.		BASE CM.	HAFT CHEST DIAM. CM.	R. M. R. PER CENT	VBP IN SEC.	CHOL. MG./100 C.C.	THYROID MEDICATION	BASAL PULSE	R. P. MIN.
					DIAM. CM.	LENGTH CM.								
12.	J. R. A. II. D.	M	63	Pre-op. 2 mo. 2½ mo. 3½ mo.	17.0 17.8 17.9 16.4	17.4 17.4 18.0 17.0	9.4 9.7 11.1 11.0	12.6 12.8 13.3 13.7	24 22 17 18	52 80 90	328 324	qs. 1, 8 daily	70 66 68	122/86 106/82 126/82
13.	F. D. R. II. D.	M	18	Pre-op. 3½ mo.	15.9 16.7	17.0 17.4	12.9 11.6	13.6 13.9	12 36	31 34	172 323		80 80	120/66 120/80
14.	W. D. R. II. D.	M	22	Pre-op. 1 mo. 3 mo. 5 mo. 8 mo. 9 mo.	17.7 17.0 17.2 18.4 16.9 16.5	17.7 17.0 17.2 18.4 16.9 16.5	13.0 11.6 15.1 14.8 14.7 13.4	15.0 14.6 15.1 14.8 14.7 14.7	8 32 27 24 19 26	51 57 41 48 35 66	92 140 152 283 170 204	qs. 1, 8 daily qs. 1, 8 daily	65 72 80 72 66	132/90 120/76 110/62 130/88 130/88
15.	B. Z. R. II. D.	F	45	Pre-op. 1 mo. 3 mo. 6 mo. 8 mo.	17.3 17.3 18.0 17.6 17.6	18.3 17.2 17.6 17.6 17.6	13.7 13.2 12.3	13.2 13.8 13.4 13.3 13.5	5 30 30 27 20 21	30 31 33 38	167 214		50 45 56 54 60	150/62 120/72 112/78 118/60
16.	B. C. R. II. D.	F	35	Pre-op. 1 mo. 2 mo. 3½ mo.	14.6 14.5 13.4 14.5	15.0 16.4 13.7 14.2	12.6 12.1 10.8 11.2	12.7 12.8 13.1 13.2	1 33 19 27	23 25 32 26	145 280 317		76 76 60 74	108/80 110/80 112/90

TABLE I—CONT'D

17.	W. B. A. P. A. H. D.	M	63	Pre-op. 3 mo.	14.7 14.5	16.0 17.7	10.9 9.2	15.0 15.3	-10 -41	18 23	117 428	65 52	122/76
18.	L. M. R. H. D.	M		Pre-op. 1 mo. 3 mo. 5 mo.	18.1 17.6 17.8 17.8	19.7 18.8 19.2 18.5	13.6 12.8 11.6 13.7	15.8 15.8 15.9 16.0	+ 6 -34 -30 -26	42 42 42 38	135 345 400	84 66 78 70	110/56 110/80 130/95 134/86
19.	E. M. H. H. D.	F	50	Pre-op. 2 mo.	18.6 18.0	18.4 17.4	11.2 11.0	14.8 14.7	- 4 -23	21 22	366	78 64	168/98
20.	B. R. R. H. D.	F	48	Pre-op. 1½ mo.	19.3 18.2	19.5 18.4	14.7 12.3	13.8 14.1	+ 3 -14	33 30	404	72 92	172/110 148/80
21.	J. T. H. H. D.	M	59	Pre-op. 5½ mo.	17.3 16.0	18.0 16.0	13.2 12.3	14.1 14.2	- 3 -20	57 29	330	58 65	140/80 148/86
22.	R. D. R. H. D. C. A.	M	22	Pre-op. 3 wk. 1 mo. 2½ mo. 3½ mo.	26.5 25.0 25.1 23.2 24.3	23.1 23.6 24.7 23.5 21.9	17.9 15.8 16.0 15.2 15.3	15.8 16.0 16.0 15.8 16.2	- 3 -30 -37 -32 -27	43 48 71 66 32	109 203	55 50 52 52 48	140/70 106/62 132/70 110/78 118/72

gr. ⅓ daily

CHANGES IN THE SEVEN-FOOT ROENTGENOGRAM

The relationship of the degree of hypothyroidism to the changes in the seven-foot roentgenogram is summarized in Table I. Cases are arranged in the order of decreasing changes in cardiac transverse diameter. The first group comprised twenty-two patients with congestive failure due to various types of heart disease (Table I). The heart size and electrocardiograms, preoperatively, showed varying deviations from the normal. In twenty of these cases the transverse cardiac diameter was greater than one-half the internal chest diameter. Following thyroidectomy, the transverse cardiac diameter increased more than 0.5 cm. in fifteen patients, showed no change in three patients and decreased more than 0.5 cm. in four patients. The greatest increase in size was

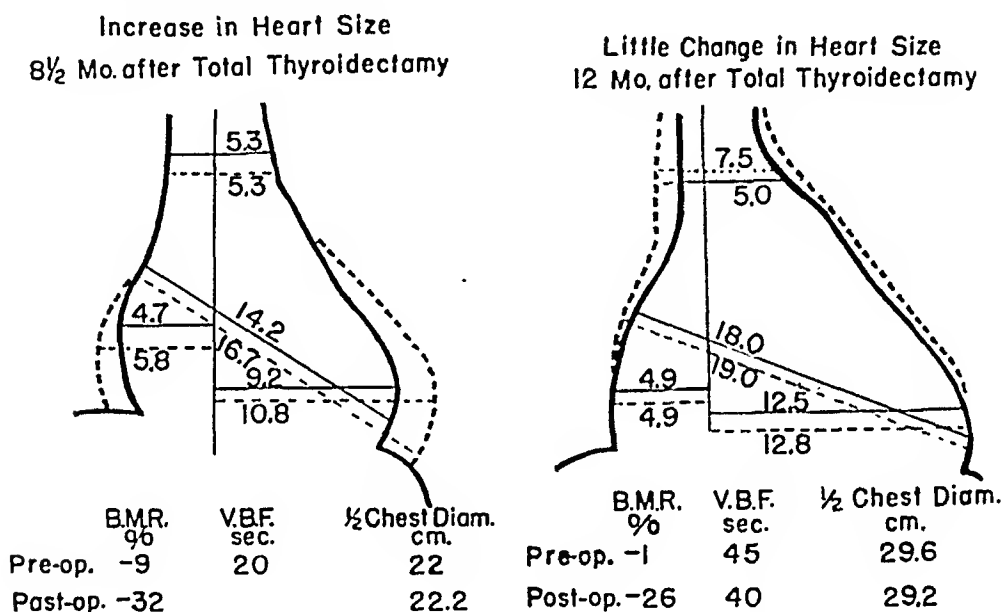


Fig. 1.—Silhouettes of heart before and after operation in Case 1. Black line represents preoperative cardiac outline; dotted line, silhouette twelve months after operation.
Fig. 2.—Silhouettes of heart before and after operation in Case 11. Black line represents pre-operative cardiac outline; dotted line, silhouette twelve months after operation.

2.7 cm.; the greatest decrease in size was 1.4 cm. The changes in heart size observed in the group with congestive failure were the resultant of two opposing tendencies: the increase in cardiac size that takes place in myxedema, and the shrinkage in heart size that accompanies the return to compensation of a heart previously decompensated. This shrinkage varied with the degree of dilatation previously present because of heart failure. According to whether one tendency or the other predominated, the heart size of the different patients in this group with congestive failure decreased, increased, or showed little or no change. (Figs. 1, 2, and 3.)

The second group comprised ten patients with angina pectoris and one patient with angina pectoris produced by paroxysmal auricular

fibrillation (Table II). In five cases the transverse cardiac diameters, preoperatively, were greater than one-half the internal chest diameters. After operation eight patients showed an increase of 0.5 cm. or more in the transverse cardiac diameter, coincident with the drop in metabolism, and three showed no change.

The third group comprised patients with no heart disease (Table III). Three of the four patients showed an increase in the transverse cardiac diameter, the greatest increase being 2.8 cm. (Case 34).

THE RELATION OF CHANGES IN HEART SIZE TO CHANGES IN THE BASAL METABOLIC RATE

The basal metabolic rate gradually decreased after total thyroidectomy, the maximum decrease occurring usually between the third and

Decrease in Heart Size
5½ Mo. after Total Thyroidectomy

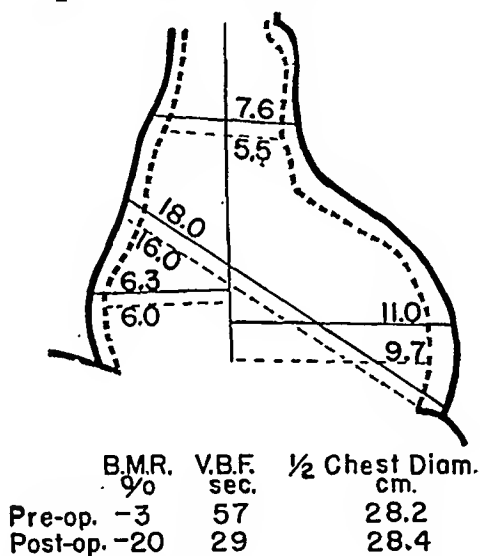


Fig. 3.—Silhouettes of heart before and after operation in Case 21. Black line represents preoperative cardiac outline; dotted line, silhouette five and one-half months after operation.

the eighth week. An increase in heart size was observed as early as the third week after operation, at which time the metabolic rate had not yet reached its lowest level (Cases 4 and 26). The increases in heart size following thyroidectomy usually developed coincident with the gradual lowering of the basal metabolic rate. Changes in measurements of the length and base of the heart usually corresponded with changes in the transverse cardiac diameter. Case 3 showed an increase of 0.7 cm. as the basal metabolic rate dropped from plus 5 to minus 22 per cent. With a further drop to minus 27, and later to minus 34 per cent, the cardiac diameter showed progressive increases of 1.6 and 2.3 cm. respectively over the preoperative values. In Case 10 there was an increase of 1 cm. as the basal metabolic rate dropped from plus 9 to

TABLE II

RELATIONSHIP OF BASAL METABOLIC RATE, VELOCITY OF BLOOD FLOW AND BLOOD CHOLESTEROL TO CHANGES IN THE SEVEN-FOOT ROENTGENOGRAM OF THE HEART IN PATIENTS WITH ANGINA PECTORIS BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT. DIAG.	SEX	AGE	TIME INT.	TRANS.		BASE CM.	HALF CHEST DIAM. CM.	H. M. R. PER CENT	VBF IN SEC. ONDS	CHOL. MG./100 C.C.	THYROID MEDICATION	BASAL PULSE	B. P. MM.
					DIAM. CM.	CARDIAC LENGTH CM.								
23.	M. G. R. H. D. A. P.	F	37	Pre-op. 1½ mo.	19.5 22.5	20.3 21.0		13.5 13.5	+3 -11	18 27			80 60	110/60
24.	S. F. A. P. Cor.	M	52	Pre-op. 1½ mo. 2 mo.	17.3 17.6 19.6	18.4 18.2 18.2	10.4 11.3 11.3	15.5 15.5 15.5	-20	23 19	234	gr. ¼ daily	76 66	
25.	A. B. A. P.	M	59	Pre-op. 1½ mo. 3 mo. 6½ mo. 9½ mo.	11.2 12.9 13.3 12.9 13.1			14.5 14.7 14.3 14.4 14.4	-8 -18 -30 -31 +12	24 18 21 25 22	211		63 69 58 72 64	140/80 132/78 138/80 140/60 138/80
26.	M. H. A. P.	M	54	Pre-op. ½ mo.	16.2 18.1	17.5 17.6	11.3 10.7	15.6 16.0	+5 -5	20 20			70 60	180/110 152/92
27.	M. W. A. P. Cor.	M	54	Pre-op. 1½ mo. 5½ mo.	10.4 11.8 11.9	15.2 14.8 15.4	10.4 7.9 10.4	14.3 14.7 14.7	-8 -18 -34	19 23 34	119 284 262		72 75 70	118/76 130/60 120/80
R. H. D.—Rheumatic heart disease H. H. D.—Hypertensive heart disease										A. H. D.—Arteriosclerotic heart disease A. P.—Angina pectoris				
										B. A.—Bronchial asthma Cor.—Healed coronary thrombosis				

TABLE II—CONT'D

NO.	INIT. DIAG.	SEX	AGE	TIME INT.	TRANS.		BASE CM.	HALF CHEST DIAM. CM.		B.M.R. PER CENT	VBF IN SEC- ONDS	CHOL. MG./100 C.C.	THYROID MEDICATION	BASAL PULSE	B. P. MM.
					CARDIAC DIAM. CM.	LENGTH CM.									
28.	G. O. A. P. B. A.	M	65	Pre-op. 1½ mo. 5½ mo.	13.4 15.6 14.9	15.6 17.6 16.8	10.2 9.9 10.0	15.5 15.5 15.0	15.4 322 280	-13 -28 -30	15 31 21	154 322 280		68 80 66	136/76 136/80 130/84
29.	R. S. A. P.	F	57	Pre-op. 3½ mo. 4 mo.	11.3 12.2 12.3	13.5 13.7 13.2	9.3 9.5 9.7	13.4 13.7 13.2	292 555	+ 3 -16 - 4	16 21 24	292 555		88 64 66	210/72 166/80 138/88
30.	M. C. A. P.	M	57	Pre-op. 1½ mo.	13.4 14.0	13.8 15.8	10.3	15.0 14.4	192 347	-24 -34	16 18	192 347		70 80	140/82 136/80
31.	M. V. A. P. A. H. D. H. H. D.	F	59	Pre-op. 1 mo. 3 mo. 6 mo.	13.6 13.6 13.9 13.5	14.7 14.6 14.9	9.0 9.1 8.9	13.0 13.4 12.9 13.2	231	-12 -22 -31 -26		231		80 72 78 68	172/66 122/88 130/88 140/90
32.	E. P. A. P. A. H. D. H. H. D.	F	59	Pre-op. 1½ mo. 5 mo.	13.4 13.4 14.0	13.8 14.0 15.0	8.1 9.8 9.1	12.7 13.1 12.9	298 482 479	-23 -27 -33	19 25	298 482 479	gr. ¼ daily	60 72 60	146/80 138/90 146/90
33.	M. F. A. P. Cor.	M	48	Pre-op. 1 mo. 5½ mo.	15.3 15.1	16.2 16.5	11.1 11.9	15.9 15.7		-14 -16 -33	18 17 31			60 64 88	140/96 140/60

TABLE III

RELATIONSHIP OF BASAL METABOLIC RATE, VELOCITY OF BLOOD FLOW AND BLOOD CHOLESTEROL TO CHANGES IN THE SEVEN-FOOT ROENTGENOGRAM OF THE HEART IN PATIENTS WITHOUT HEART DISEASE BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT. DIAG.	SEX	AGE	TIME INT.	TRANS.		BASE CM.	HALF CHEST DIAM. CM.		B. M. R. PER CENT	VLF IN SEC. ONDS	CHOL. MG./100 C.C.	THYROID MEDICATION	BASAL PULSE	B. P. MM.
					CARDIAC DIAM. CM.	LENGTH CM.									
34.	H. M. C.	M	63	Pre-op.	8.7			13.8		+ 1	15	168		84	
				1 mo.	11.1	14.1	9.3	13.6		-21	20	320		76	
				3 mo.	11.5	13.6	10.3	13.8		-31	20	305		84	
				5½ mo.	10.2	14.0	10.0	13.8		-10	23			72	120/80
				8 mo.	11.5			14.0			19	301	gr. 1 t.i.d. for 7d.		
35.	F. F.	M	52	Pre-op.	13.4	16.8	10.1	14.8		0	22			68	
				3 wk.	13.1	15.9	13.1	15.0		-13	17			70	
				2½ mo.	14.7			15.2		-25	31			70	
36.	M. A.	F	19	Pre-op.	7.8	12.0	8.6	11.0		- 7	14			88	110/66
				2 mo.	8.7	12.2	9.2	11.6		-41		400		72	90/60
				3½ mo.	8.8	13.0	9.1	11.4		0	13	269	gr. ¼ daily	84	110/90
37.	M. D.	F	24	Pre-op.	11.0			14.7		+10	9			80	110/68
				2 mo.	10.9	13.0	12.2	12.8		-32	14			78	
										-34	17		gr. ¼ daily		

minus 15 per cent. In Case 11 the basal metabolism remained exceptionally constant from the first to the twelfth month after operation. During this time the transverse diameter showed no marked changes, although with the initial lowering in metabolic rate during the first postoperative month the heart size had increased appreciably. The administration of small doses of thyroid, as indicated in Tables I, II, and III, caused a prompt decrease in heart size in some patients.

In patients with congestive failure increased heart size did not always parallel lowering in the metabolic rate. With clinical improvement, and consequently lessened cardiac dilatation, the heart sometimes became smaller. In patients with angina pectoris, however, and in those patients with congestive failure who had reached the stage of compensation, changes in the metabolic rate were usually accompanied by corresponding changes in heart size (Table I). In Case 4 the basal metabolic rate had dropped from plus 9 to minus 36 per cent by the end of the fourth postoperative week, and the transverse cardiac diameter had increased 2.2 cm. Two weeks later, after thyroid medication, the basal metabolic rate had increased to minus 23 per cent, and the transverse cardiac diameter had shrunk 1.2 cm. below its one month diameter. Similar responses were seen in Cases 14 and 8.

In some instances (Cases 5, 7, and 29) the basal metabolic rate was not markedly lowered in patients who showed definite clinical manifestations of hypothyroidism. In these cases the changes in heart size corresponded to the degree of hypothyroidism as indicated by the elevated serum cholesterol values and by the clinical findings.

RELATION OF CHANGES IN ELECTROCARDIOGRAMS TO THE DEVELOPMENT OF THE HYPOTHYROID STATE

The electrocardiographic changes following total thyroidectomy have been observed in thirty-two patients (Tables IV, V, VI). The case numbers correspond with those of Tables I, II, and III. The voltages of the R- and T-waves in all three leads are recorded. The T-wave measurements represent the greatest voltage above and below the base line. The electrical axis was calculated according to the method of Einthoven and showed no significant variations. Changes in the voltage of T-waves in some cases are partly attributable to varying degrees of digitalization and of coronary and myocardial disease. Minor variations in the P-R and QRS intervals in a few instances may be related to the same factors. Definite diminution in the amplitude of the ventricular complexes which could not be attributed to the above factors was evident in twenty-four of the thirty-two patients studied. In these patients diminution in amplitude generally appeared with the first significant drop in the metabolic rate (Cases 1, 3, and 4). The greatest change occurred with the maximum development of hypothyroidism. In these cases the P-R and QRS interval usually showed no change after operation.

TABLE IV—CONT'D

NO.	INIT.	SEX	AGE	RATE PER MIN.	P-R INT. SEC.	QRS INT.	VOLTAGE IN MILLIVOLTS					B. M. R. PER CENT	TIME INTERVAL
							R ₁	R ₂	R ₃	T ₁	T ₂	T ₃	
7.	F. Z.	M	19	80 80	0.24 0.26 0.24	0.11 0.12 0.13	1.20 2.20 1.50	0.70 1.30 0.60	0.50 0.90 0.50	+0.10 +0.20 -0.30	+0.20 +0.20 0.40	0.15 0.20 0.50	Pre-op. 2 weeks 3½ months
8.	S. Be.	F	51	110 85 80 90	A. F. A. F. A. F. A. F.	0.04 0.04 0.04 0.06	0.40 0.20 0.30 0.20	1.50 0.80 1.00 0.70	1.10 0.70 0.90 0.60	0.10 0.10 0.00 0.05	-0.15 -0.15 -0.15 -0.05	-0.15 -0.15 -0.15 -0.07	Pre-op. 1 month 3 months 4 months
10.	W. B.	M	55	80 70 60 75	0.16 0.14 0.16 0.16	0.07 0.07 0.07 0.06	1.30 1.00 1.20 1.00	1.50 1.40 1.20 1.20	0.35 0.35 0.30 0.30	-0.05 0.00 0.00 -0.05	-0.20 -0.17 -0.18 -0.15	-0.15 -0.10 -0.10 -0.15	Pre-op. 1 month 2 months 7 months
11.	G. F.	M	52	80 50 65 60 90	A. F. A. F. A. F. A. F. A. F.	0.08 0.06 0.06 0.07 0.06	0.70 0.90 0.80 0.60 0.60	0.90 0.80 0.70 0.50 0.60	0.40 0.30 0.30 0.20 0.20	0.25 0.15 0.10 0.05 0.00	0.25 0.15 0.15 0.00 0.05	0.00 -0.10 -0.05 0.00 0.00	Pre-op. 2 months 5 months 10 months 12 months
12.	J. R.	M	63	80 70 80	A. F. A. F. A. F.	0.08 0.08 0.07	1.50 1.60 0.80	0.20 0.00 0.00	0.00 0.00 0.00	-0.20 -0.15 +0.06	0.00 0.10 0.05	0.20 0.20 0.10	Pre-op. 2 months 3 months
13.	F. D.	M	18	95 80 100	A. F. A. F. A. F.	0.05 0.08 0.08	0.20 0.30 0.30	0.80 0.80 0.90	0.80 0.90 1.00	0.10 -0.10 0.10	-0.15 +0.10	-0.10	Pre-op. 4 months 5 months
14.	W. D.	M	22	75 75 60 65	0.22 0.21 0.25 0.20	0.08 0.08 0.07 0.08	0.30 0.15 0.20 0.10	0.65 0.75 0.75 0.90	0.80 0.60 0.55 0.70	0.15 0.05 0.00 +0.05	0.20 0.10 +0.10 +0.10	+0.05 0.00 +0.05 +0.05	Pre-op. 1 week 1 month 9 months

TABLE IV—CONT'D

NO.	INIT.	SEX	AGE	RATE PER MIN.	P-R INT. SEC.	QRS INT.	VOLTAGE IN MILLIVOLTS						B. M. R. PER CENT	TIME INTERVAL
							R ₁	R ₂	R ₃	T ₁	T ₂	T ₃		
15.	B. Z.	F	45	70 59 55 65 60	A. F. A. F. A. F. A. F. A. F.	0.08 0.08 0.08 0.08 0.06	0.30 0.10 0.10 0.10 0.10	1.00 0.70 0.60 0.50 0.50	1.30 0.80 0.80 0.70 0.70	+0.05 0.00 -0.05 -0.00 -0.10	-0.20 -0.15 -0.15 -0.10 -0.15	-0.10 -0.10 -0.05 0.00 -0.05	-5 -30 -20 -21	Pre-op. 1 month 1½ months 6 months 8 months
16.	B. C.	F	35	70 120 70 70	A. F. A. F. A. F. A. F.	0.06 0.06 0.06 0.08	0.30 0.40 0.40 0.40	0.80 0.60 0.70 0.60	0.50 0.40 0.40 0.30	0.10	0.15	0.15	-1 -33 -19 -27	Pre-op. 1 month 2 months 4 months
17.	W. B.	M	63	65 75	0.16 0.17	0.04 0.06	0.08 0.40	0.40 0.20	0.00 0.00	0.15 -0.10	0.13 -0.15	0.00 0.00	-10 -41	Pre-op., 3 months
18.	L. M.	M	55	90 70 90 90	0.20 0.20 0.20 0.18	0.12 0.12 0.12 0.12	0.40 0.30 0.50 0.40	0.10 0.00 0.00 0.00	0.00 0.00 0.00 0.00	+0.05 -0.10 0.00 0.00	0.00 0.00 0.00 0.07	0.05 0.00 0.10 0.05	+6 -30 -26	Pre-op. 2 weeks 3 months 5 months
20.	B. R.	F	48	85 70	A. F. A. F.	0.06 0.06	1.00 1.10	1.00 1.00	0.10 0.10	0.10 -0.15	0.15 0.00	0.13 0.10	+3 -14	Pre-op. 2 months
21.	J. T.	M	59	120 90 65	A. F. A. F. A. F.	0.12 0.12 0.08	0.60 1.10 0.50	0.00 0.00 0.00	0.00 0.00 0.00	-0.10 -0.20 -0.05	0.20 0.25 0.10	0.30 0.40 0.15	-3 -28 -20	Pre-op. 2 months 6 months
22.	R. D.	M	22	90 70 70 70	A. F. A. F. A. F. A. F.	0.08 0.08 0.08 0.08	0.80 0.60 0.60 0.60	1.50 1.00 0.95 1.00	1.00 0.90 0.70 0.70	-0.10 ±0.05 ±0.05 -0.10	0.15 0.20 0.15 0.06	0.15 0.10 0.20 0.10	-3 -30 -32 -27	Pre-op. 3 weeks 2 months 4 months

*A. F.—Auricular fibrillation.

TABLE V

RELATIONSHIP OF BASAL METABOLIC RATE TO CHANGES IN THE ELECTROCARDIOGRAM IN PATIENTS WITH ANGINA PECTORIS BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT.	SEX	AGE YEARS	RATE MIN.	P-R INT.		QRS INT. SEC.	VOLTAGE IN MILLIVOLTS							B. M. R. PER CENT	TIME INTERVAL
					SEC.	SEC.		R ₁	R ₂	R ₃	T ₁	T ₂	T ₃			
25.	A. B.	M	59		0.17		0.08	0.70	1.20	0.60	0.10	0.25	0.00	- 8	Pre-op. 2 weeks	
				85	0.18	0.08	0.50	1.10	0.60	0.00	0.15	0.05				
				90	0.17	0.09	0.40	0.90	0.50	0.00	0.05	0.00				
				80	0.18	0.09	0.50	0.90	0.60	0.07	0.10	0.10				
26.	H. K.	M	58	75	0.20		0.11	0.60	0.90	0.80	0.10	0.15	0.10	-17	Pre-op. 2 weeks	
				60	0.20	0.12	0.60	0.60	0.30	0.05	0.10	0.03				
27.	M. W.	M	54		0.20		0.06	0.35	0.10	0.10	±0.05	0.05	0.10	- 7	Pre-op. 2 weeks	
				80	0.18	0.08	0.30	0.20	0.20	0.00	0.03	0.00				
				75	0.16	0.08	0.40	0.10	0.10	0.05	0.00	0.00				
					0.16	0.06	0.35	0.10	0.10	0.03	0.05	0.05				
28.	G. O.	M	65		0.22		0.06	0.40	0.20	0.00	0.00	0.10	0.10	-13	Pre-op. 1 month	
				70	0.20	0.04	0.20	0.30	0.00	0.00	0.10	0.10				
				80	0.21	0.06	0.40	0.30	0.00	0.00	0.00	0.05				
				85	0.21	0.06	0.40	0.30	0.00	0.00	0.00	0.05				

TABLE V—CONT'D

NO.	INIT.	SEX	AGE YEARS	RATE MIN.	P-R INT. SEC.	QRS INT. SEC.	VOLTAGE IN MILLIVOLTS					B. M. R. PER CENT	TIME INTERVAL
							R ₁	R ₂	R ₃	T ₁	T ₂	T ₃	
30.	M. C.	M	57	85	0.20	0.06	0.60	0.60	0.00	±0.05	0.05	0.00	Pre-op. 24
				100	0.20	0.06	0.60	0.40	0.00	±0.10	-0.10	-0.05	26
				100	0.16	0.06	0.40	0.20	0.00	0.05	0.05	0.00	32
				100	0.16	0.06	0.40	0.60	0.00	0.05	0.10	0.00	32
31.	M. V.	F	59	65	0.16	0.08	2.00	1.50	0.80	0.15	0.15	-0.13	Pre-op. 12
				90	0.16	0.07	1.40	1.20	0.50	±0.10	0.05	0.00	22
				85	0.16	0.07	1.10	1.70	0.50	±0.15	0.08	0.10	31
32.	E. P.	F	58	60	0.18	0.08	0.90	0.30	0.25	0.20	0.25	0.00	Pre-op. 23
				85	0.20	0.06	0.80	0.00	0.20	0.10	0.10	0.00	27
				85	0.18	0.06	0.60	0.15	0.15	0.15	0.10	0.00	2 months
				70	0.18	0.08	0.50	0.10	0.20	0.10	0.15	0.10	5 months
33.	M. F.	M	48	70	0.16	0.06	1.50	0.90	0.10	-0.20	-0.10	0.10	Pre-op. 14
				80	0.16	0.06	1.20	0.50	0.00	0.05	0.00	0.00	16
				60	0.16	0.06		1.10			-0.10		27
				70	0.16	0.08	1.10	0.80	0.00	0.03	0.03	0.00	33
				75	0.14	0.06	0.70	0.40	0.00	0.00	0.00	0.00	36

TABLE VI

RELATIONSHIP OF BASAL METABOLIC RATE TO CHANGES IN THE ELECTROCARDIOGRAM IN PATIENTS WITHOUT HEART DISEASE BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT.	SEX	AGE YEARS	RATE MIN.	P-R INT. SEC.	QRS INT. SEC.	VOLTAGE IN MILLIVOLTS						B. M. R. PERCENT	TIME INTERVAL
							R ₁	R ₂	R ₃	T ₁	T ₂	T ₃		
36.	W. M.	M	63	105	0.16	0.08		0.80			0.25		+ 1	Pre-op.
				65	0.20	0.07		0.40			0.00		-31	3 months
				80	0.16	0.08	0.30	0.60	0.40	0.00	0.20	0.10	-10	6 months
				70	0.16	0.06	0.40	0.40	0.20	0.00	0.00	0.00		8 months
37.	F. F.	M	52	100	0.20	0.06		0.40			0.10		0	Pre-op.
				70	0.21	0.06		0.50			0.10		-13	3 weeks
				75	0.20	0.07		0.20			0.00		-25	3 months
38.	M. D.	F	24	100	0.18	0.06	1.00	1.30	0.30	0.20	0.20	0.00	+10	Pre-op.
				100	0.16	0.04	0.40	0.80	0.50	0.00	-0.05	-0.05	-32	2 months
39.	R. M.	M	14	95	0.16	0.07	1.60	0.60	0.10	0.30	0.15	-0.10		Pre-op.
				85	0.16	0.08	1.30	0.60	0.00	0.15	0.10	-0.05	-47	1½ months

THE RELATION OF THE VELOCITY OF BLOOD FLOW TO THE BASAL METABOLIC RATE AND TO THE SIZE OF THE HEART

The slowing in velocity of blood flow which generally occurs concomitant with lowering in the basal metabolic rate has been previously described.⁶⁻⁹ The same relation was evident in patients with angina pectoris and in the subjects without heart disease. (Tables II and III.) In patients with congestive failure in whom the velocity of blood flow before operation was slow, the development of the hypothyroid state was frequently accompanied by a further slowing in the velocity of blood flow. The significance of this, in relation to the clinical improvement shown by these patients, has been discussed in a previous communication.⁹

Of twenty-two patients with congestive failure fifteen showed a correlation between the changes in heart size and the velocity of blood flow. In eight of these fifteen patients the transverse diameter of the heart increased and the velocity of blood flow slowed; in five patients the velocity of blood flow remained slow and the heart size did not change. In two patients the velocity of blood flow increased and the heart became smaller.

BASAL HEART RATE AND BLOOD PRESSURE BEFORE AND AFTER
THYROIDECTOMY

Changes in blood pressure and heart rate after total thyroidectomy were variable and striking only in occasional cases.^{5, 7} Of thirty-three patients with either congestive failure or angina pectoris eleven showed a decrease, and seven an increase, in heart rate of ten or more beats; fifteen showed changes of less than ten beats per minute (Table VII).

TABLE VII
CHANGES IN BASAL HEART RATE AND BLOOD PRESSURE BEFORE AND
AFTER TOTAL THYROIDECTOMY

	HEART RATE	SYSTOLIC B.P.	DIASTOLIC B.P.
<i>Results in 22 patients with congestive failure</i>			
Decreased	6	10	3
No change	11	9	12
Increased	5	1	5
Insufficient data	0	2	2
<i>Results in eleven patients with angina pectoris</i>			
Decreased	5	3	2
No change	4	6	6
Increased	2	0	1
Insufficient data	0	2	2

The above data were analyzed on the basis of changes in heart rate of ten beats or more; changes in systolic blood pressure of 20 mm. or more; and diastolic pressure of 10 mm. or more.

Thirteen patients showed a decrease, and one showed an increase in systolic blood pressure of 20 mm. of mercury or more. Fifteen showed changes of less than 20 mm. of mercury in the systolic pressure. In

four patients data were insufficient. Five patients showed a decrease, and six an increase in diastolic blood pressure of 10 mm. or more of mercury. Eighteen showed changes less than 10 mm. of mercury in the diastolic pressure.

RELATIONSHIP OF CHANGES IN HEART SIZE AND ELECTROCARDIOGRAPH VOLTAGE TO CARDIAC FUNCTION IN PATIENTS WITH ANGINA PECTORIS AND CONGESTIVE FAILURE BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

The significance of changes in heart size, basal metabolic rate, electrocardiographic tracings, and velocity of blood flow as expressions of the hypothyroid state has been briefly reviewed. That such changes do not result in impairment in cardiac function has been shown by the striking improvement coincident with the development of the hypothyroid state in patients who, before operation, suffered from chronic heart disease. Objective measurements of the degree of functional improvement in such patients have also been made. A modified Master and Oppenheimer exercise tolerance test²⁴ was performed by patients with congestive failure before and at varying intervals after thyroidectomy. Patients with angina pectoris undertook similar exercise under the standardized conditions elsewhere described.³² After the development of the hypothyroid state patients with congestive failure showed a more normal response of blood pressure and heart rate to the same or greater increments of exercise than was evident before operation (Table VIII). Patients who showed marked dyspnea and collapse on exercise before operation experienced little or no distress when the test was repeated after thyroidectomy. Similarly, patients with angina pectoris no longer experienced attacks of chest pain on exercise under conditions which invariably produced anginal attacks before operation, in spite of increases in heart size and diminution in voltage of the electrocardiographic tracings (Table IX). The tests outlined herein are examples of many others to be published in forthcoming publications. The increased capacity for exercise demonstrated by these patients usually paralleled the slowing of the velocity of blood flow as the basal metabolic rate fell.

DISCUSSION

In previous communications the treatment of intractable heart disease by total thyroidectomy was demonstrated as a feasible and effective procedure in patients without clinical or pathological evidence of hyperthyroidism. From previous studies the conclusion had been drawn that by reducing the basal metabolism in patients with heart disease one would lessen the metabolic and circulatory demands of the individual so that the previously reduced circulation would become adequate to the decreased needs of the body.

TABLE IX

RELATIONSHIP OF CHANGES IN HEART SIZE, ELECTROCARDIOGRAPHIC VOLTAGE, BASAL METABOLIC RATE AND VELOCITY OF BLOOD FLOW TO CARDIAC FUNCTION IN PATIENTS WITH ANGINA PECTORIS BEFORE AND AFTER TOTAL ABLATION OF THE NORMAL THYROID GLAND

NO.	INIT.	SEX	AGE	TIME INTERVAL	TRANS- VERSE CARD. DIAM.	HALF CHEST DIAM.	VOLTAGE		B. M. R. PER CENT	VBF IN SEC.	NO. OF TRIPS	RESULT OF EXERCISE
							R.	T.				
1.	A. B.	M	59	Pre-op. 6½ mo.	11.2 12.9	14.5 14.4	1.2 0.8	0.25 0.0	- 8 -31	24 25	58-73 419	Angina No angina
2.	G. O.	M	65	Pre-op. 5½ mo.	13.4 14.9	15.5 15.0	0.2 0.3	0.1 0.0	-13 -30	15 21	21-21 50	Angina No angina
3.	R. S.	F	57	Pre-op. 3½ mo.	11.3 12.2	13.4 13.7			+ 3 -16	16 22	29-30 60	Angina No angina
4.	M. W.	M	54	Pre-op. 5½ mo.	10.4 11.9	14.3 14.7	0.1 0.1	0.5 0.5	- 8 -34	19 35	13-15 75	Angina No angina

The same considerations of supply and demand for blood underlie the rationale for total ablation of the thyroid for relief of angina pectoris. When the work of the heart is augmented, as in exercise, there must be a rise in coronary circulation. If, because of arteriosclerotic narrowing of the coronary vessels or other causes, the coronary circulation cannot increase in accord with the increased needs of the heart, anoxemia develops and angina pectoris ensues.²⁵ After the development of hypothyroidism following total thyroidectomy, the heart at rest requires less coronary blood flow and can therefore withstand a greater increment of work before reaching the upper limit of circulation set by the relatively fixed coronary vessels.

Since the inception of this work twenty patients with angina pectoris and forty-five patients with various types of congestive failure have undergone operation. With the development of hypothyroidism, most of these patients have shown definite clinical evidence of relief of congestive failure and angina pectoris, notwithstanding changes in heart size and electrocardiographic voltage characteristic of hypothyroidism.

The foregoing observations on artificial myxedema after total thyroidectomy in patients with congestive failure have shown that the changes in heart size are evidently the result of two opposite factors: (1) the effect of the hypothyroid state tending to increase the size of the heart; (2) the restoration of circulatory compensation tending to decrease the size of the heart. The heart size of the individual patients in this group decreased or increased according to which factor predominated. In some patients the two opposing tendencies evidently counterbalanced each other, for the heart size remained unaltered. These variable changes are in contrast to the almost invariable tendency of the heart to increase in size in patients with spontaneous myxedema who had no congestive failure.²¹ Similarly electrocardiographic changes typical of myxedema were present in only fourteen of twenty patients with congestive failure.

In patients with angina pectoris in whom the factor of shrinkage of the heart with restoration of circulatory compensation was not operative, and in patients without heart disease in whom artificial myxedema was produced, increased heart size and diminished voltage in electrocardiographic tracings occurred more often. Eight of eleven patients with angina pectoris showed an increase in heart size, and three no change. Three of four patients without heart disease showed these changes.

In this study the character, rate, and extent of development of changes in heart size and electrocardiographic voltage coincident with the development of the hypothyroid state could be followed from the time of their first appearance. By means of simultaneous observations of the basal metabolic rate, blood cholesterol, velocity of blood flow, and development of clinical signs and symptoms of myxedema, it was possible

to study accurately the degree of hypothyroidism. It became evident on the basis of these indices that the rate and extent of development of change in heart size and electrocardiographic voltage paralleled the development of the hypothyroid state. These changes were usually not progressive over periods of study as long as three to twelve months if the metabolism was maintained at about minus 30 per cent by the administration of thyroid. Our observations indicate that the increase in heart size and diminution in voltage of the R- and T-waves in the electrocardiogram which occur in myxedema are an accompaniment and an intrinsic characteristic of the hypothyroid state rather than a secondary consequence of myxedema.

These studies also demonstrate clearly that "myxedema heart" in the sense of circulatory failure does not exist as a necessary accompaniment of the hypothyroid state. Most of the subjects of this study had suffered serious cardiovascular disease over an extended period of time and so might have been expected to show more readily any further impairment of cardiac function due to the development of myxedema. In the presence of increased cardiac size and diminished voltage of the electrocardiogram, however, signs and symptoms of congestive failure, rather than becoming more prominent in these patients, disappeared. That the increased cardiac size due to hypothyroidism does not subsequently cause functional impairment is shown by an analysis of the clinical course of patients months after operation. The course of the patients who showed the greatest increase in heart size is of particular interest. Although Patient 1 showed the greatest increase in the transverse cardiac diameter (2.7 cm.), she has experienced striking clinical improvement during the twelve months since total thyroidectomy. Prior to operation she was confined to bed, having had rheumatic heart disease with attacks of congestive failure over a period of twenty-six years. At the time of writing, twelve months after total thyroidectomy, her capacity for work is unmistakably greater than at any time since operation. She is able to perform household duties without dyspnea, is no longer orthopneic, and at no time has evidenced the signs or symptoms of congestive failure. Case 2 was a twenty-seven-year-old man with rheumatic heart disease, hemoptysis for seven years, and attacks of congestive failure for five years. This patient was a cardiac invalid for three years prior to operation. Six months after operation, in spite of an increase in heart size of 2.1 cm., this patient was up and about from eight to ten hours a day without evidence of return of congestive failure. Case 4 was a sixty-six-year-old man with syphilis, arteriosclerotic heart disease, and congestive failure of six years' duration, who had been confined to bed or chair for four years. Eight months after operation, in spite of daily activity, this patient has shown no evidence of congestive failure. This patient showed x-ray and electrocardiographic

changes typical of hypothyroidism. It is apparent that the cardiac enlargement occurring in these patients concomitant with the development of hypothyroidism has not impaired cardiac function.

A similar conclusion may be drawn from a study of the reaction of these patients to exercise. Prior to operation patients with congestive failure performing standard exercise tolerance tests exhibited marked dyspnea, collapse, and an abnormally slow return of blood pressure and pulse to normal after the termination of exercise. After operation, in the face of increased cardiac size and diminution in electrocardiographic voltage, they were able to accomplish even more work with little or no dyspnea and with a more normal physiological response of blood pressure and pulse. Likewise, patients with angina pectoris no longer experienced attacks of pain on exertion in spite of teleroentgenographic and electrocardiographic changes typical of hypothyroidism. One may conclude, therefore, that "myxedema heart" in the sense of a condition aggravating or precipitating attacks of congestive failure or angina pectoris does not exist in patients with induced hypothyroidism in whom the basal metabolic rate is maintained at about minus 30 per cent.

SUMMARY AND CONCLUSIONS

1. Observations are presented concerning the rate and character of changes in heart size in thirty-seven patients, and changes in electrocardiographic voltage in thirty-two patients in whom artificial myxedema was produced by total ablation of the normal thyroid gland. These patients were observed from one and one-half to twelve months after operation.

2. The degree of the hypothyroid state was estimated by measurements of the basal metabolic rate, velocity of blood flow, blood cholesterol, and the signs and symptoms of myxedema. Changes in heart size and electrocardiographic voltage were interpreted on the basis of these indices.

3. After total thyroidectomy, fifteen of twenty-two patients with congestive failure showed an increase of more than 0.5 cm. in the transverse cardiac diameter, three showed no change, and four showed a decrease of more than 0.5 cm. Of eleven patients with angina pectoris eight showed an increase in heart size and three no change; of four patients with no heart disease three showed an increase in heart size and one no change.

4. The variations in changes in heart size in the patients who had congestive failure before operation were the result of two opposing factors: (1) the effect of the hypothyroid state tending to increase heart size; (2) the restoration of circulatory compensation tending to decrease heart size.

5. Observations on the changes in the electrocardiographic voltage

of P- and T-waves in thirty-two patients gave the following results: of twenty patients with congestive failure fourteen showed a decrease, five no change, and one an increase in voltage; of eight patients with angina pectoris five showed a decrease and three no change in voltage; of four patients without heart disease all showed a decrease in voltage.

6. The rate and extent of increase in the heart size and of decrease in electrocardiographic voltage of these patients paralleled the development of the hypothyroid state and were a manifestation rather than a secondary consequence of myxedema. These changes generally showed no progression when the metabolism was fixed at a given decreased level by thyroid medication, and regressed if the metabolism was raised significantly.

7. In spite of these changes in heart size and electrocardiogram, the patients studied showed a disappearance of signs and symptoms of congestive failure or of angina pectoris with persistence of improvement from three to twelve months, and increased capacity for work as measured by standard exercise tolerance tests.

8. "Myxedema heart" in the sense of a condition aggravating or precipitating attacks of congestive failure or angina pectoris does not develop when hypothyroidism is produced by total ablation of the normal thyroid gland in patients whose metabolism is maintained at about minus 30 per cent.

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THE DETERMINATION AND THE SIGNIFICANCE OF THE AREAS OF THE VENTRICULAR DEFLECTIONS OF THE ELECTROCARDIOGRAM*†

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IT IS the purpose of this article to describe a method of analyzing the electrocardiogram which has not been employed hitherto and which yields information not obtainable in other ways. This method is based upon the measurement in suitable units of the areas of the electrocardiographic deflections in the three standard leads. The data so obtained are used to determine the mean electrical axis of the heart during the inscription of the QRS deflections, of the T deflection, and of the ventricular complex as a whole. The mean electrical axis during the inscription of the auricular complex may be determined by the same method.

Methods. We may illustrate this method by applying it to the electrocardiogram reproduced in Fig. 1, which is a characteristic example of the curves seen in bundle-branch block of the common type. In this instance two string galvanometers were employed, and Leads II and III were each recorded simultaneously with Lead I. The original curves, taken on film, were enlarged approximately six diameters by projection. The ventricular complex as it appeared in each lead was then traced (Fig. 2) on thin paper by following the lower margin of the string shadow with a sharp pencil. Due care was taken to place each of the three tracings in its proper relation to the zero level, represented by the horizontal line HH' , and to the vertical line VV' , which marks the beginning of the QRS interval.

It is desirable that the areas of the electrocardiographic deflections should be expressed in units that do not vary in value with the film speed or with the string sensitivity employed in recording individual curves. The larger rectangles defined by the vertical and horizontal co-ordinates in Fig. 1 are 5 mm. in height and extend lengthwise over an interval of 0.2 second. Since the introduction of one millivolt into the string circuit produced a deflection of exactly one centimeter, the area of each of these rectangles is equivalent to that of a deflection 100 micro-

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volts in amplitude and one second in duration, or to 100 microvolt-seconds (m.v.s.). The smaller rectangles are each equivalent to four such units of area. After tracing each ventricular complex the corners of the projected image of one of the larger rectangles lying in the same vertical section of the film were marked by small dots, which were subsequently connected by straight lines. Only two such rectangles appear in Fig. 2, because in this instance the even spacing of the time lines made a third unnecessary.

When the tracings were completed, they were mounted on cardboard to prevent creeping of the thin paper, and two vertical lines were drawn, one at the end of the QRS interval and the other at the end of the ventricular complex. The area of QRS and the area of T in each lead were then measured with an accurate planimeter. In measuring the

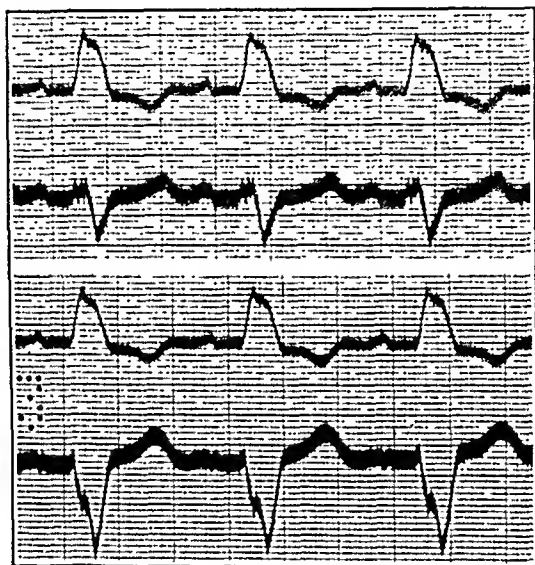


Fig. 1.—Standard electrocardiogram of the type seen in bundle-branch block of the common variety. Upper record: Lead I and Lead II. Lower record: Lead I and Lead III.

former we began at the intersection of the baseline with the line (VV') which represents the beginning of the QRS interval, and followed the outline of the curve until the line that marks the end of the QRS interval was reached. This line was then followed to the baseline, and the latter was traced back to the starting point. In measuring the area of T we began at the intersection of the baseline with the line that marks the end of the QRS interval. Passing along this last line to its junction with the outline of the curve, we followed the latter to the end of the ventricular complex and returned along the baseline to the point of beginning. This method of measurement gives the net area; i.e., those portions of the area that lie below the baseline and are considered negative and those that lie above the baseline and are considered positive are added algebraically by the planimeter. The area of QRST, the

ventricular complex as a whole, was obtained by algebraic addition of the area of QRS and the area of T. All areas were then expressed in microvolt-seconds by dividing each of them by one one-hundredth of the area, measured by planimeter in square millimeters, of the large rectangle traced from the corresponding part of the film, and have been arranged in tabular form (Table I).

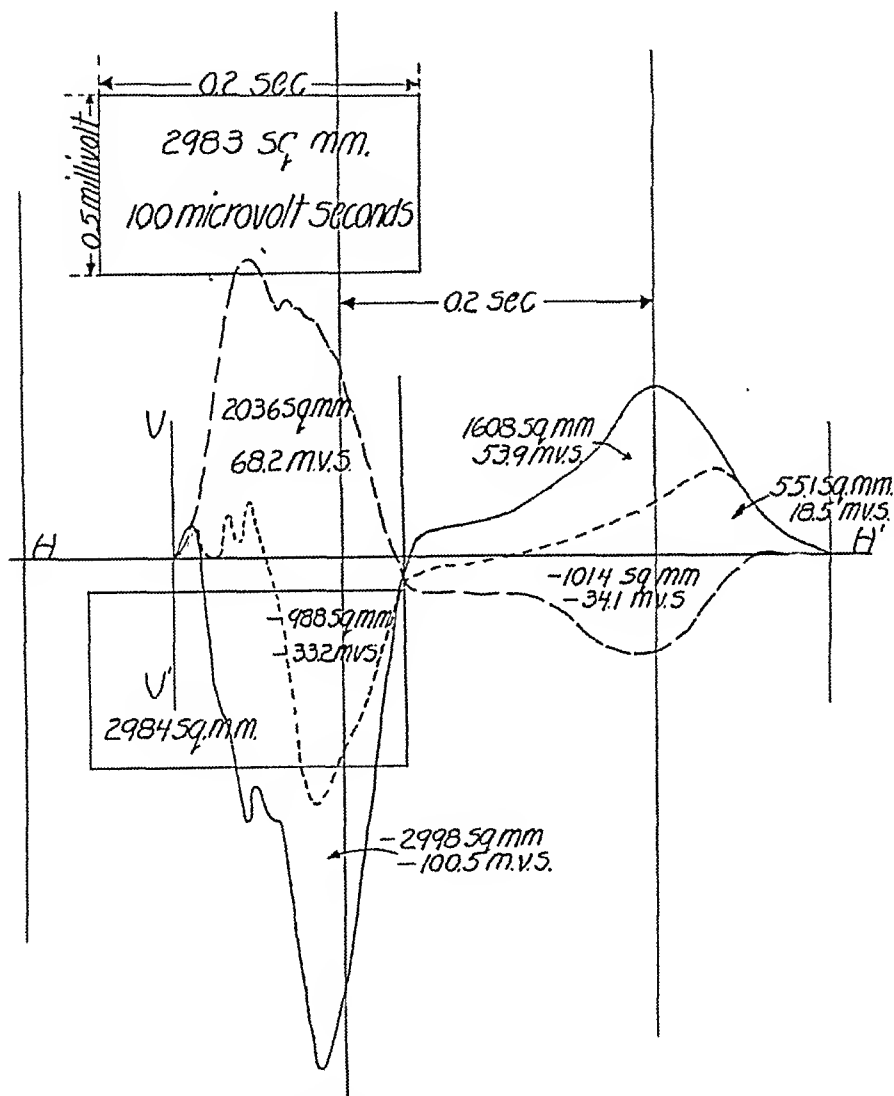


Fig. 2.—Tracings of the ventricular complexes of the curves shown in Fig. 1. The area measurements were made with a planimeter.

TABLE I*

	I	II	III	ANGLE	MANIFEST AREA
QRS	67.3	-33.2	-100.5	-49	102.5
T	-35.7	18.5	54.2	130	55.0
QRST	31.6	-14.7	-46.3	-48	47.2

*Areas in microvolt-seconds of the ventricular deflections of electrocardiogram shown in Fig. 1.

In cases in which the curves have been inaccurately standardized, the appropriate corrections must, of course, be made. It is clear that the area of any deflection or group of deflections in Lead II must equal the sum of the areas of the deflections inscribed in Leads I and III during the same interval. This rule is a necessary consequence of Einthoven's equation, which states that at any instant the deflection in Lead II must equal the sum of the deflections in the other two leads. It is very useful as a check upon the accuracy of the area measurements. It is not essential that two or more leads be taken simultaneously; the method described may be successfully applied when the three leads are taken in rotation in the ordinary way. When this is done, curves which show large respiratory variations in the form of the ventricular complex should be avoided. Otherwise, it may be necessary to measure several complexes in each lead in order to obtain figures in accord with the rule mentioned. In many instances we have made enlarged photographic prints, instead of tracings, of the original curves, and this method is to be preferred as the more accurate. The prints should be mounted to prevent curling. The proper location of the baseline is a matter of the greatest importance. A slight error in placing this line may be responsible for a large error in the measurement of the area of the T-wave which rests upon a broad base. It is therefore best not to attempt to measure curves in which the baseline shifts or in which, for some other reason, its position cannot be exactly determined.

The mean electrical axis and the manifest area. Einthoven and his associates¹ have shown that the resultant electromotive force developed by the heart at any instant may be represented by an electric dipole or doublet located at the center of an equilateral triangle. The right arm, left arm, and left leg are represented by the apices of this triangle, and the three standard electrocardiographic leads by its three sides. The position of the axis of the doublet, which may be referred to as the instantaneous electrical axis of the heart, is defined by the angle α which it makes with the side of the triangle corresponding to Lead I. The potential difference that this doublet would produce in a given lead if its axis were parallel to the corresponding side of the triangle is referred to as E , the manifest potential difference. If a segment of length E is laid off upon the electrical axis, the deflections in the three leads will be given by the projections of this segment upon the three sides of the triangle. When the deflections in any two leads are known, the angle α and the manifest potential difference may be determined by several methods.

If, in like manner, we represent the mean electromotive force developed by the heart during the QRS interval by a doublet at the center of Einthoven's triangle, the axis of this doublet may be referred to as the mean electrical axis of QRS. We may lay off on this axis a seg-

ment E equal in magnitude to the manifest area of QRS; i.e., the area of the QRS deflections that would be inscribed in a given lead if the mean electrical axis were parallel to the corresponding side of the triangle. The projections of this segment upon the sides of the triangle will then give the area of QRS in each of the three leads. If the area of QRS is known for any two leads, the inclination of the mean electrical axis of QRS and the manifest area of QRS are easily found. The mean electrical axis of T, the manifest area of T, the mean electrical axis of QRST, and the manifest area of QRST may be defined in the same way and may be found by the same methods. From the center of Einthoven's triangle as origin three vectors, representing QRS, T and QRST, respectively, may then be drawn in such a way that each vector will give the position of the mean electrical axis and the magnitude of the manifest area of the corresponding deflection or group of deflections. The

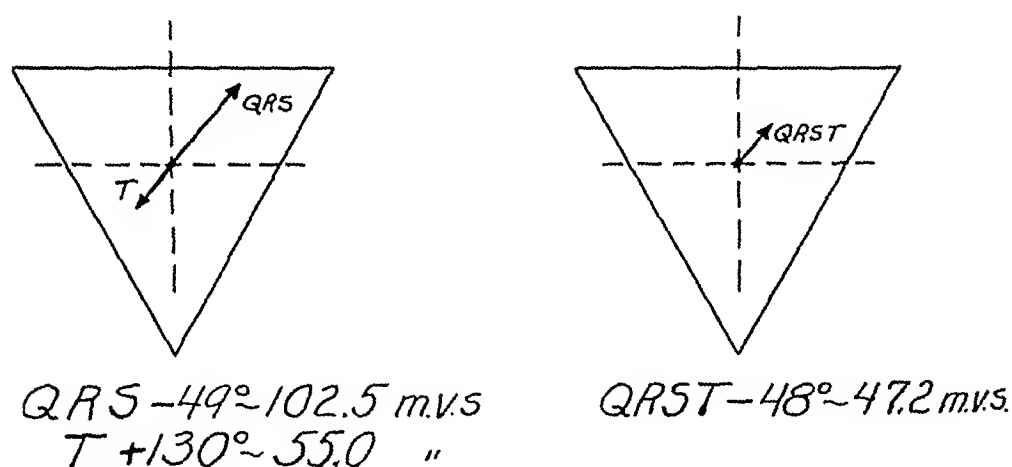


Fig. 3.—The position and relative length of the vectors which represent the mean electrical axis of QRS, of T, and of QRST in Fig. 1.

last of these vectors is the vector sum of the other two. The vectors which represent the QRS, T and QRST deflections of the electrocardiogram reproduced in Fig. 1 are shown graphically in Fig. 3. The angles, which define the directions, and the manifest areas, which give the lengths of these vectors, are set down in Table I in line with the measured areas from which they are derived. It will be noted that although the mean electrical axis of T is separated from that of QRS by an angle of approximately 180 degrees, the manifest area of T is only a little more than half as great as that of QRS. For this reason the mean electrical axis of QRST and the mean electrical axis of QRS have approximately the same direction.

The mean electrical axis and the manifest area of any deflection or group of deflections may be determined with approximately the same accuracy as the electrical axis and manifest potential difference at a given instant. There is no fundamental difference between the method

followed in the determination of the former and that employed in the determination of the latter. Both methods rest upon the same foundations and involve the same assumptions. The mean and the instantaneous electrical axis are both resultants and both involve a process of vectorial summation; the former differs from the latter in that the summation extends over a time interval.

Significance of the mean electrical axis. The significance that is attributed to the mean electrical axis naturally depends upon the interpretation that is placed upon the instantaneous electrical axis. We shall adopt the view, originally advanced by Lewis,² that at any instant during the QRS interval the electrical axis points in the direction in which the excitatory process is at that moment spreading along the average ventricular muscle fiber.

This view, which is strongly supported both on the experimental and on the theoretical side^{2, 3, 4} advances two distinct and independent postulates. The first of these has to do with the manner in which the electrical forces produced by the various muscle units composing the ventricles are to be summed in order to find their resultant. It is held that so far as the potential differences produced in the three standard leads are concerned, the component electrical forces may each be represented by a vector and may be added vectorially or according to the parallelogram law. The electrical axis of the heart is determined in accordance with this principle, and the assumptions that permit us to add the electrical forces produced in different parts of the heart as if they were vectors are the same as those upon which Einthoven's equilateral triangle is based. In other words, it is assumed that for practical purposes we may consider the apices of the triangle distant and equidistant from all parts of the heart and that we may consider the body a homogeneous conductor.

The second postulate has to do with the relation between the orientation of the electrical forces associated with the wave of excitation and the direction in which this wave is moving. If a constant relation of this kind exists, it must follow that at any instant the effective force produced by a muscle fiber is fully determined within that portion of the fiber which is in the process of passing from the resting to the active state. The extent and position of the remaining portions of the fiber are immaterial. It is implied that if two adjacent elements of a muscle fiber differ in their state of activity, one being nearer to or farther from the resting state than the other, there must be an electromotive force across and normal to the plane that separates them.

Theoretical effects produced by a muscle fiber suspended in air. Bearing these postulates in mind, we may attempt to evaluate the more important factors that determine the areas of the electrocardiographic de-

flections. This purpose will be most easily accomplished by discussing theoretical experiments upon single cardiac muscle fibers. It will be convenient to employ the terminology of the so-called membrane theory, and to assume in accordance with this theory that a resting muscle fiber is surrounded by a polarized* membrane which is partly or completely depolarized when the fiber becomes active, and is repolarized when the fiber returns to the unexcited state.

Let us first consider a curve of the kind obtained by leading directly from muscle strips removed from their natural surroundings and suspended in air. Imagine that it were possible to isolate a single cardiac muscle fiber and place it in contact with two nonpolarizable electrodes

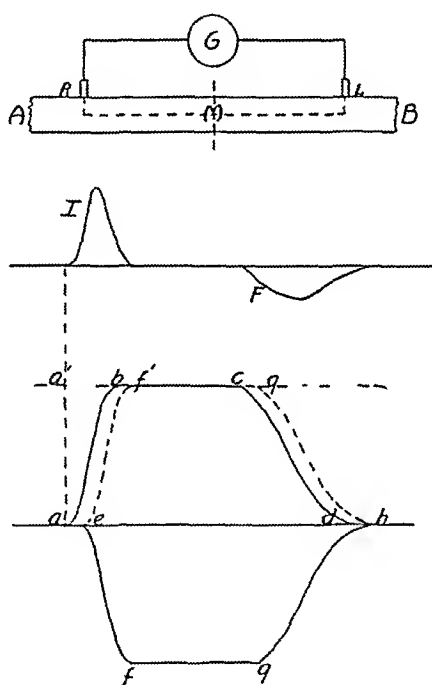


Fig. 4.—Diagram illustrating the electrical effects produced by excitation of a muscle fiber suspended in air.

arranged as in Fig. 4 and connected to the terminals of a sensitive galvanometer or electrometer. For our present purpose we may disregard such complications as arise from the presence of a film of fluid on the outside of the fiber and consider the electromotive force in the galvanometer circuit proportional to the electromotive force in the circuit *GRMLG*, and therefore to the difference between the intensity of

A membrane or surface may be referred to as polarized when it displays equal and opposite electrical properties on its two sides. A muscle element is polarized when it exhibits equal and opposite properties at its two ends. If a polarized body is placed in an electric field in such a way that the lines of force and the direction in which the body is polarized are perpendicular, the intensity to which a given element of the body is polarized is measured by the moment of the couple acting upon that element divided by the product of its volume and the strength of the field. In the case of a polarized membrane or surface the intensity of polarization may be defined as the electrical moment per unit area per unit strength of field. Across a polarized surface there is an electromotive force proportional to the intensity of polarization.

polarization beneath the electrode at R and the intensity of polarization beneath the electrode at L . If the intensity of polarization is the same at both points, this electromotive force will be zero; if it is less beneath one electrode, that electrode will be relatively negative with respect to the other.

It should be observed that in effect there is an electromotive force across every boundary that defines a difference in the intensity of polarization. If for example, a plane through M divides the muscle membrane into two parts, one of which is polarized to an intensity P_1 and the other to an intensity P_2 , the electromotive force in all leads from the external surface will be the same as if a surface coinciding with that portion of the specified plane lying inside the fiber were polarized to an intensity $P_2 - P_1$. Where there is a gradient in the intensity of polarization over a given portion of the fiber, the effect is the same as if that portion of the fiber were polarized in a direction parallel to the axis of the fiber.

If the electrodes (Fig. 4) are sufficiently close together, the curve recorded when the muscle is stimulated at A will consist of a sharp initial deflection (I) corresponding to the QRS deflections of the ventricular complex, and a broader final deflection (F) corresponding to the T-wave. This diphasic curve may be considered the algebraic sum of two monophasic curves, one of which ($abcd$) represents the curve that would be obtained if the passage of the excitation wave produced no change in the intensity of polarization beneath the electrode at L , and the other ($efgh$) the curve that would be obtained if it produced no change in the intensity of polarization beneath the electrode at R . The first of these monophasic curves would actually be recorded if the excitatory process were initiated at A and blocked between R and L . If the excitation wave were blocked between L and B , the second could be obtained by transferring the electrode at R to the latter point. If the electrodes are so close together that depolarization is complete at L before repolarization begins at R , the initial deflection (I) of the diphasic curve may be ascribed to the depolarization, the final deflection (F) to the repolarization process.

It is easily shown that if, as a result of the passage of the wave of depolarization or the wave of repolarization along the fiber, the intensity of polarization changes in the same manner and to the same extent beneath both electrodes, the area of the resulting deflection is proportional to the magnitude of the change and to the time required by the process producing it to spread from the first electrode to the second, but does not depend upon the form of the curve that represents the manner in which the change takes place. We may sum the two monophasic curves algebraically by reversing the sign of the second ($efgh$) and subtracting the ordinates of the resulting curve ($ef'g'h$) from those of

the first ($abcd$). The area of the initial deflection (I) of the diphasic curve will then be represented by the area $abf'e$ and the area of the final deflection (F) by the area $cg'h'd$. If the curve ab and the curve ef' are alike in form, the first of these areas is equal to that of a rectangle of which aa' is one side and ae the other; if the curve cd and the curve $g'h$ are alike in form, the second area is equal to that of a rectangle of which aa' is one side and dh the other. It is therefore clear that, provided it does not change from point to point, the form of the curve that represents the manner in which depolarization takes place cannot affect the area of the initial deflection I . If the form of the curve that represents repolarization does not vary, it cannot affect the area of the final deflection F .

The sum of the areas of the initial and final deflections (I and F) of the diphasic curve must be equal to the sum of the areas of the two monophasic curves ($abcd$ and $efgh$). If the areas of the latter are alike in absolute magnitude, the area of F must be equal in magnitude but opposite in sign to the area of I , and the sum of these areas must be zero. This sum must always measure the difference in absolute magnitude between the two monophasic curves; if it is not zero, we may conclude that the curve $abcd$ and the curve $ef'g'h$ differ in form. There is then a difference between the changes in the intensity of polarization produced by the excitation process at R and those produced by this process at L . Such a difference in the behavior of the muscle beneath the two contacts must depend chiefly, if not entirely, upon factors that do not affect the muscle as a whole but act upon it locally.

Excitation at R may differ from excitation at L either as regards the magnitude of the change in the intensity of polarization produced, the duration of the excited state, the form of the curve that represents depolarization, or the form of the curve that represents repolarization. A large difference in the magnitude of the change in the intensity of polarization must produce pronounced displacement of that segment of the diphasic curve which is inscribed immediately after the initial deflection (I) ends. In our subsequent discussion we shall assume that no such displacement is present and shall speak of the effects produced by local variations in the excitatory process as if they were due solely to a gradient affecting the duration of the excited state; in other words, to a difference between the velocity of the wave of depolarization and the velocity of the wave of repolarization. There is no apparent reason for supposing that the sum of the areas of the two monophasic curves and, therefore, of the initial and final deflections of the diphasic curve is dependent upon the point of stimulation or upon the distance between the electrodes.

Theoretical effects produced by a muscle fiber immersed in a conducting medium. We may think of a muscle fiber as made up of an arbitrary

number of muscle units or elements placed end to end, and of the effects produced by excitation of a muscle fiber as the sum of the effects produced by excitation of the elements of which it is composed. The electromotive force generated by a single element at a given instant is proportional to the difference in the intensity of polarization at its two ends. We may regard the curve $abcd$ (Fig. 4) as representing the changes in the intensity of polarization that take place during excitation at one end of the element and the curve $ef'g'h$ as representing the changes that occur, after an interval ae , at the other end. The electromotive force generated by the element will then be represented by the curve IF . The difference in potential between two electrodes in contact with a muscle fiber suspended in air is proportional to the algebraic sum of the electromotive forces generated by all the muscle units lying between the electrodes. Upon this potential difference the electromotive forces generated by the other elements of the fiber have no effect.

If, however, the muscle fiber is immersed in an extensive conducting medium, the situation is entirely different. Every muscle element producing an electromotive force will then contribute in some measure to the potential difference between the electrodes, which may be placed in contact with the fiber or merely in contact with the medium in which it is immersed. The electromotive force produced by a given element may be represented by a dipole or doublet located inside the element and so placed that its axis coincides with that of the muscle fiber. The strength of this doublet must be made proportional to the cross-sectional area of the element, to its length, and to the difference in the intensity of polarization at its two ends. If the medium about the fiber is sufficiently extensive, the effect of the doublet upon the potential of an electrode at any point will vary inversely as the square of the distance from the electrode to the element and directly as the cosine of the angle between the axis of the doublet and the line drawn from the electrode to the center of the element.

Assuming that the relative position of the electrode and the muscle element does not change, the only variable factor among those that determine the effect exerted by the latter upon the potential of the former is the difference in the intensity of polarization at the two ends of the element. Since this varies in accordance with the curve IF (Fig. 4), this curve may be regarded as representing the variations in potential of a single electrode, or the variations in the difference in potential between two electrodes, produced by the excitation of a single muscle element. Every curve obtained from a single fiber or from a group of fibers must therefore represent the algebraic sum of a very large number of curves of this type, varying one from another in sign, in amplitude and in phase. We may, therefore, conclude that the sum of the areas of the initial and final deflections of any curve which represents

the excitation of the ventricular muscle is a measure of the effects produced by local variations in the excitatory process, and particularly by local variations in the duration of the excited state.

Effects produced by a muscle fiber located at the center of Einthoven's triangle. Let us suppose that the immersed fiber lies in the wall of the heart, and therefore at the center of Einthoven's triangle. For all practical purposes the electrodes at the apices of this triangle may then be regarded as equidistant from all the fiber elements. We may therefore represent the doublet generated by a given element at a given instant by a vector coinciding in direction with the axis of the doublet and pointing from the negative to the positive pole. The length of this vector must be made proportional to the strength of the doublet at the given instant. The doublet represented by the sum of all the vectors generated by the different elements of the fiber will then represent the electromotive force produced at that moment by the fiber as a whole.

If each elementary vector is given a length proportional to the product of a given interval and the mean electromotive force produced by the corresponding element during that interval, the resultant vector will coincide in direction with the mean electrical axis of the fiber during the given interval and will have a length proportional to the manifest area of the deflections produced by the activities of the whole fiber during that period. If the fiber is of such a length that depolarization of all its elements is complete before repolarization begins at any point, the deflections produced by depolarization and those produced by repolarization will be separable. The areas of the two sets of deflections in the three leads corresponding to the sides of the triangle will then furnish the data necessary for the determination of three vectors representing, respectively, the effects produced by depolarization, the effects produced by repolarization, and the effects produced by local variations in the excitatory process. The last of these vectors will be the sum of the other two.

If the cross-sectional area of the fiber is uniform, the vector which represents the effects produced by depolarization will coincide in direction with, and will have a length proportional to, the sum of the two vectors drawn from the point where the fiber first becomes active, the point of stimulation, to its two ends. This is true whether the fiber is straight or curved. If there are no local variations in the excitatory process, the inverse of this vector will have the same direction and the same relative length as that derived from the areas of the deflections produced by repolarization.

As an example of the effects produced by local variations in the excitatory state, consider those produced by a uniform gradient in the duration of the excited state. The vector which represents the effects produced by this gradient will point from the end of the fiber where

systole is longer toward the end where it is shorter, and will have a length proportional to the difference in the length of systole at the two ends. Neither the direction nor the length of this vector will be affected by the location of the point of stimulation.

An illustration may perhaps contribute to the understanding of the principles involved. Let AB (Fig. 5) represent a muscle fiber of uniform cross-sectional area lying in the wall of the heart at the center of Einthoven's triangle. If this fiber is stimulated at C , the effects produced by depolarization will be represented by CD , which is the sum of the vectors CA and CB ; the projections of CD upon the three sides of the triangle will be proportional to the areas of the deflections produced in the three leads by the depolarization process. Suppose that there is a uniform gradient in the duration of the excited state of such kind

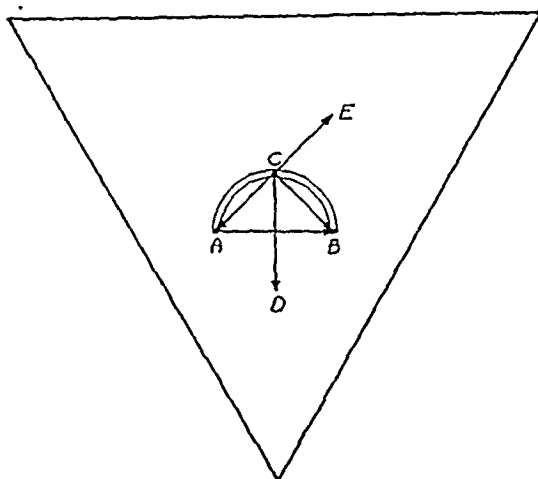


Fig. 5.—Diagram illustrating the electrical effects produced by a muscle fiber lying in the body at the center of Einthoven's triangle (see text).

that systole is longer at A than at B by an amount equal to the time required by the depolarization process to spread from A to B . The time required by the repolarization process to spread from C to A against the gradient (in the direction in which the systole increases in length) will then be double that required by the wave of depolarization, and the effects produced by repolarization of this segment of the fiber will be represented by the vector AE which is twice as long as CA and opposite in direction. The time required by the repolarization process to spread from C to B (in the direction in which systole decreases in length) will be zero, for repolarization will begin at C and at B at the same time. The repolarization of this segment of the fiber will therefore produce no effects whatsoever. The effects produced by the gradient will be represented by AB , the vector sum of AE and CD . The projection of the vector AB upon any side of the triangle will be proportional to the sum of the areas of all the deflections produced in the corresponding lead by repolarization and depolarization of the muscle fiber.

It would be possible to extend this discussion to much more complicated cases, but space is not available for that purpose. We have endeavored to make clear the course of reasoning which has led us to the following conclusions: The mean electrical axis of the QRS deflections gives the direction, so far as it can be represented in the plane of Einthoven's triangle in which the depolarization process spreads over the average element of ventricular muscle. The mean electrical axis of T gives the inverse of the direction in which the repolarization process

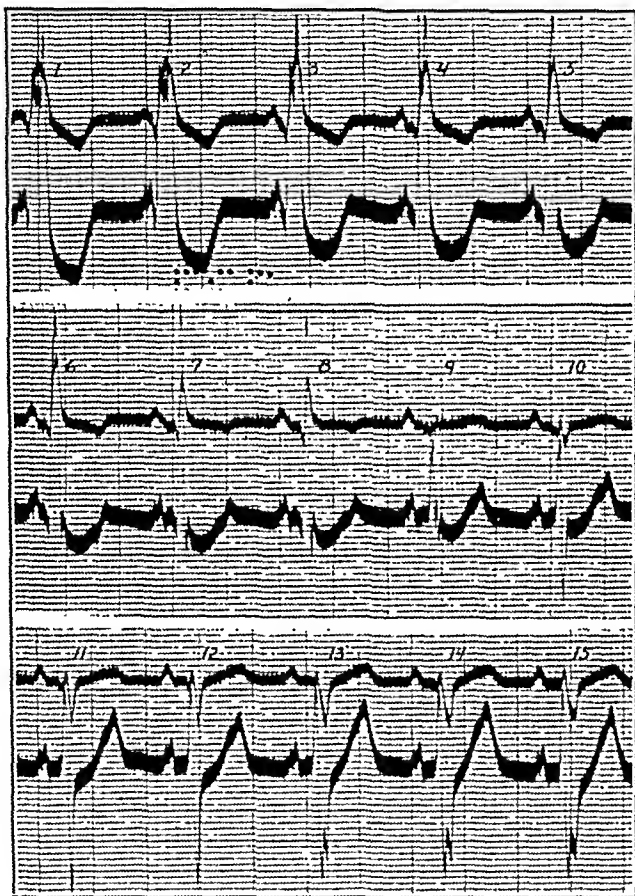


Fig. 6.—A continuous record showing the ventricular complexes referred to in Table II. This series of complexes was obtained by rhythmic stimulation of the central region of the right ventricle after cutting the right branch of the His bundle. Lead I is shown above and Lead III below.

spreads over the average element of ventricular muscle. The manifest area of QRST is a measure of the effects produced by local variations in the excitatory process, and the mean electrical axis of QRST gives the direction of the line along which these variations are greatest. The conclusion that the manifest area and the electrical axis of QRST are determined by local variations in the excitatory process and are not affected by the order in which the various portions of the ventricular muscle pass into the excited state was tested in the following way: A large dog was anesthetized, and the heart was exposed by splitting the

sternum and opening the pericardial sac. The right branch of the His bundle was cut, in the usual way, and the characteristic changes in the form of the ventricular complex were obtained. The central region of the right ventricle was then stimulated rhythmically at a rate only slightly different from the heart rate. In this way a series of ventricular complexes, transitional in form between the complexes of right branch block, and those of the opposite type produced by right ventricular stimulation, were recorded (Fig. 6). Leads I and III were taken simultaneously, and the areas of QRS and T were measured. These areas and the data derived from them are shown in Table II.

It was anticipated that the area of QRST, in both leads, the manifest area of QRST and the mean electrical axis of QRST would remain nearly constant.

The observed variations in these quantities are shown in the table. It will be seen that they are of an irregular kind and show no relation to the form or the area of QRS. They are probably explained by errors in measurement due chiefly to improper placement of the baseline, to the movements of the heart produced by rhythmic inflation of the lungs, and to a lack of uniformity in the movements of the ventricular muscle when contracting. It should also be pointed out that slight variations in the form of the T-wave often occur from beat to beat without obvious cause; these are due, in all probability, to variations in the factors responsible for local peculiarities in the excitatory state.

In judging the significance of the observed variations in the area of QRST, it must be remembered that this area is obtained by the algebraic addition of the area of QRS and the area of T, and is often very small in comparison with the absolute magnitude of the area that must be measured to determine its value. In the case of Complex 2 (Table I) the area of QRST in Lead III was found to be 36.5 m.v.s. The mean value of the area of QRST in this lead was 25.0 m.v.s. The difference between the maximum value (36.5) and the mean value (25.0) is, therefore, approximately 50 per cent of the latter. The former value (36.5) was, however, obtained by measuring the area of QRS, which amounted to 136.0 m.v.s., and the area of T, which amounted to 99.5 m.v.s., a total area of 235.5 m.v.s. An error of 5 per cent in the determination of this total area would therefore account for the maximal variation in the area of QRST above its mean value observed in Lead III. The maximum variation below the mean value (Complex 10) is less easily accounted for. When everything is taken into consideration, however, the data obtained in this experiment will be seen strongly to support the view that the area of QRST is determined by local variations in the excitatory process, and is not dependent upon the area of QRS, which is determined by the order of ventricular excitation.

TABLE II

COMPLEX NO.	LEAD I AREA IN M.V.S.				LEAD III AREA IN M.V.S.				MEAN ELECTRICAL AXIS ANGLE IN DEGREES				MANIFEST AREA IN M.V.S.			
	Qrs	T	QRST		Qrs	T	QRST		Qrs	T	QRST		Qrs	T	QRST	
1	47.3	-36.0	11.3		132.0	-107.0	25.0		75	-104	72		186.0	149.0	37.0	
2	44.7	-35.2	9.5		136.0	-99.5	36.5		76	-105	79		188.0	140.0	48.8	
3	40.0	-25.2	14.8		106.0	-82.1	23.9		75	-103	68		152.0	112.0	39.2	
4	34.2	-21.9	12.3		98.5	-71.0	27.5		76	-103	72		138.0	97.5	40.7	
5	28.4	-19.0	9.4		84.1	-59.7	24.4		77	-104	74		114.0	82.0	34.8	
6	25.9	-14.0	11.9		79.2	-53.2	26.0		76	-101	72		109.5	71.2	38.7	
7	12.4	-10.9	1.5		50.0	-23.7	26.3		79	-108	87		66.1	35.3	31.2	
8	9.9	-5.3	4.6		40.8	-21.8	19.0		79	-101	79		53.8	28.8	26.1	
9	-2.2	4.9	2.7		13.9	8.7	22.6		98	69	84		15.0	13.7	27.6	
10	-6.6	6.5	-0.1		-4.4	20.6	16.2		-127	77	90		11.1	28.5	18.7	
11	-10.9	11.2	0.3		-17.2	42.7	25.5		-113	79	90		28.4	57.0	29.7	
12	-10.3	15.5	5.2		-19.1	38.5	19.4		-110	73	78		30.0	55.6	25.9	
13	-16.1	19.1	3.0		-37.2	69.2	32.0		-107	78	86		54.9	92.7	38.8	
14	-16.1	18.8	2.7		-40.7	72.5	31.8		-106	79	86		58.5	96.8	38.3	
15	-14.1	20.9	6.8		-42.1	60.1	18.0		-104	76	75		58.5	84.2	25.7	

SUMMARY

By measuring the areas of the ventricular deflections of the electrocardiogram it is possible to determine the mean electrical axis of QRS, which gives the direction in which the excitatory process spreads over the average element of ventricular muscle, and the mean electrical axis of T, which gives the inverse of the direction in which the recovery process spreads over the average element of ventricular muscle.

If all the ventricular muscle passed through the period of excitation in the same time and in the same way, the area of QRS and the area of T would be equal in absolute magnitude, but opposite in sign, and the area of QRST would be zero. The area of QRST is a measure of the electrical effects produced by local variations in the excitatory process. The mean electrical axis of QRST gives the direction of the line along which these local variations are greatest.

The local variations in the excitatory process which determine the mean electrical axis of QRST are dependent upon factors that act upon different parts of the ventricular muscle with different intensities. They are not materially influenced by the course of the excitatory process over the ventricular muscle.

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STUDIES IN RHEUMATIC HEART DISEASE

AN ANALYSIS OF 119 HEARTS WITH SPECIAL REFERENCE TO THE RELATIONSHIP OF AURICULAR FIBRILLATION TO MITRAL VALVULAR DEFORMITY AND CERTAIN RHEUMATIC TISSUE CHANGES*

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THE problem of the causation of auricular fibrillation has been approached by numerous investigators from various points of view. Anatomical studies¹⁻⁹ have demonstrated no specific lesion. Experimental and physiological studies¹⁰⁻¹⁵ have developed the idea that auricular fibrillation is essentially a functional disturbance. It is generally conceded, however, that, although it may be a functional disorder, it is found more frequently in hearts that have been structurally altered by disease than in hearts anatomically sound. More recently statistical reports have been made,¹⁶⁻²³ based mainly on clinical studies and with particular emphasis on the varied etiology and prognosis. The general consensus of opinion of these analyses has been that there is apparent no common etiological factor.

In this study the problem has been approached from a different standpoint. By making an essentially structural study of one form of heart disease, namely, rheumatic, an attempt has been made to answer certain questions: 1. What is the relationship of the occurrence of auricular fibrillation to the presence of various grades of mitral stenosis or insufficiency? 2. What relationship has the occurrence of auricular fibrillation to age at death? 3. What relation has the occurrence of auricular fibrillation to the presence and grade of mitral stenosis or insufficiency in the various decades? 4. What relationship has auricular fibrillation to active rheumatic inflammation independent of the grade of valvular deformity? 5. Is there any relationship between the occurrence of auricular fibrillation and the presence of cardiac lesions in addition to mitral valvular deformity? 6. To what extent does auricular thrombosis occur in hearts with auricular fibrillation, and is there a relationship to the degree of stenosis and active inflammation? 7. What is the mode of death of patients with auricular fibrillation, and is there any relationship to the presence of "rheumatic inflammation"?

To lend significance to the answers to these questions, a group of hearts of patients with auricular fibrillation was compared with a larger

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one of hearts of patients dying with sinus rhythm. In this way discernible differences between the two groups may become apparent.

The importance of the problem may be further inferred from the data^{24, 25} concerning the relative immunity of patients with chronic progressive valvular disease and auricular fibrillation to the development of subacute bacterial endocarditis. A similar immunity has been noted^{20, 25, 26, 27} in patients who have *severe* mitral stenosis. Our interest in the problem was stimulated by the study of a recent case²⁸ which was an exception to the former dictum. At that time we believed that a parallel which is drawn from the infrequency of the association of subacute bacterial endocarditis and advanced mitral stenosis on the one hand, and auricular fibrillation on the other, must take into account the frequency of auricular fibrillation in the various grades of mitral stenosis.

No attempt was made to duplicate the work of others who have studied the neuromuscular tissue, particularly of the sinus node, or its blood supply, or the nature of auricular lesions in various types of heart disease.

MATERIAL AND METHODS OF STUDY

One hundred and nineteen rheumatic hearts obtained at necropsy during the past thirteen years from the Third (New York University) Medical Division, Bellevue Hospital, were examined. Under this term are included those specimens exhibiting evidences of varying degrees of valvulitis in association with interstitial, vascular, or serosal inflammatory changes or their end-results, in which *no* evidence was found of any *demonstrable or specific bacterial inflammatory change or purely degenerative alterations*.

While the sample is small for purposes of accurate statistical analysis, it is large, nevertheless, when considered from the standpoint of cases coming to necropsy from one medical service.* We are using the data for the trends that analysis may reveal.

All the specimens exhibited some degree of involvement of the mitral valve. Not all were from individuals who were known to have suffered from heart disease in life. The majority (75 per cent) died of congestive heart failure; the rest of a variety of diseases. All cases of bacterial endocarditis were omitted, however, regardless of antecedent changes. Specimens of so-called pure aortic valve involvement were rejected because the etiology could not be determined. Forty-two hearts were from cases of established auricular fibrillation (not paroxysmal); of these, 36 were verified by electrocardiograms. In 27, fibrillation was present for more than one month prior to death, in some instances for several years, and in the majority for more than six months. Of the other 9 cases which had been electrocardiographed, auricular fibrillation

*With an average bed capacity of 150; material has also been drawn from the pediatrics service (average bed capacity of 140) in the past two years since its affiliation with New York University.

was observed in 7 for from one to three weeks before death; the remaining 2 patients died shortly after admission (two to six days) without a reliable history as to the approximate onset of fibrillation. For purposes of this report, 2 cases of established auricular flutter are included, one of three months' the other of one year's duration.

Sex Incidence.—Of the 42 patients with auricular fibrillation, 21 were males and 21 females. Among the 77 cases of sinus rhythm, 51 were males and 26 females. The sex incidence, therefore, is similar to that in recent clinical studies.^{21, 23, 29}

Age.—The average age at death of the 42 patients with auricular fibrillation was forty-three years; the youngest was ten, the oldest seventy years of age. The average of those with sinus rhythm was thirty-five years; the extremes were seven and eighty years. Because of limited pediatric necropsy material, the number of hearts from children was small. (Table II shows the distribution of cases according to decades.)

Incidence of Auricular Fibrillation in Mitral Stenosis.—Ninety-six of the 119 specimens exhibited some degree of mitral stenosis. In 39 (40 per cent) auricular fibrillation was present. In the clinical study of DeGraff and Lingg,²³ 50.5 per cent of their 402 rheumatic cardiac patients with mitral stenosis developed auricular fibrillation. Of 100 cases of mitral stenosis reported by Stone and Feil²⁹ auricular fibrillation occurred in 53 per cent. Weiss and Davis³⁰ in their report,* including paroxysmal auricular fibrillation or flutter, found an incidence of 57 per cent in 164 necropsied cases of "the most advanced type of rheumatic cardiac change."

Criteria for Pathological Diagnosis.—The grade of stenosis was estimated as severe, and slight to moderate. This was an arbitrary grouping, depending upon the diminution in size of the auriculoventricular orifice. We have found no single criterion or measurement satisfactory for estimating the degree of stenosis. Anyone who has attempted to establish the degree of stenosis by measurement is aware of the difficulties encountered. For example, one sees stenotic orifices which are caused by fusion of only slightly thickened cusps, the ring of the valve remaining within normal limits (Fig. 1). Conversely, one encounters

*The report by these authors deals with material which is considerably different from that presented here. Their finding of "only 66 cases of mitral stenosis of the total 164 cases of marked rheumatic heart disease" is at such variance with our data that strict comparisons may not be made. As already stated, of 119 consecutive hearts of the rheumatic type examined by at least one, and in 90 per cent by all of us, mitral stenosis was encountered in 96 cases, mitral insufficiency 7 times, and in 16 cases inflammatory disease of the mitral valve, although present, was not associated with stenosis or insufficiency of the AV orifice.

To indicate that the discrepancy is not confined to material described here, reference may be made to the anatomical studies of valvular disease of Clawson, Bell and Hartzell³¹. In a group of 166 hearts which may be termed of the rheumatic type, 18 were cases of acute rheumatic endocarditis without valvular defects; 18 were identified as recurrent rheumatic, and 130 were classified under the term old valvular defects. If 32 cases of isolated aortic valve disease and three of isolated pulmonary valve involvement are omitted on the grounds of indeterminate etiology, a group of 131 hearts is set up which may be considered examples of severe rheumatic heart disease. Of these 88 had mitral stenosis, 264 mitral insufficiency, 1 aortic insufficiency, and in the others disease produced no stenosis or insufficiency.

long, narrow, slitlike orifices in which the circumference, as a result of cicatricial shortening of the cusps, approaches that of the ring (Fig. 2). Although both measurements may be practically normal, the degree of stenosis may be severe due to scarring and fixation in position of the cusps. The final decision was based, therefore, upon all the factors contributing to anatomical diminution of the auriculoventricular orifices, such as the size of the valve opening compared to the size of the ring, the degree of approximation of the valve cusps to each other, the degree of fusion of the commissural junctions, fixation in position, and the presence or absence of free motion of the valve. (See Figs. 3 to 6.)

Fig. 1.

Fig. 2.

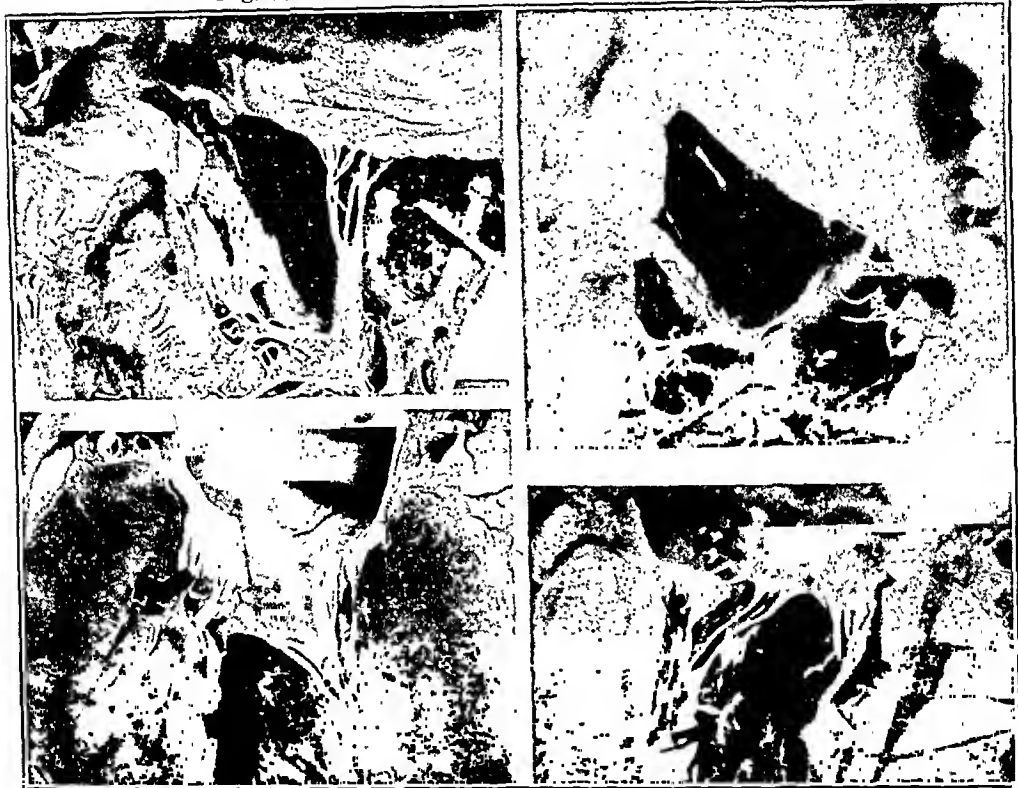


Fig. 3.

Fig. 4.

Figs. 1-4.—Severe atrioventricular valvular stenosis.

Fig. 1.—(Necropsy No. 16,573) Female, thirty-eight years. Severe "button-hole" type of stenosis of the tricuspid valve due to obliteration of the commissures by fusion of the cusps. The leaflets are only slightly thickened; the chordae tendineae are somewhat thickened but not shortened. The circumference of the valve orifice is much smaller than that of the ring.

Fig. 2.—(Necropsy No. 12,251) Female, thirty-seven years. Severe "fish-mouth" type of tricuspid stenosis due to fusion at the commissures and marked rigidity of the valve as a result of fibrosis. Because of the retraction of the leaflets with shortening, the circumference of the slitlike orifice approaches that of the ring. The chordae tendineae, most of which are not visible in the photograph, are only slightly thickened and of normal length.

Fig. 3.—(Necropsy No. 19,889) Male, fifty-three years. "Funnel" type of severe mitral stenosis with cicatricial contraction of both leaflets as well as their chordae tendineae. Although there is some retraction of the cusps, the orifice is markedly diminished because of the complete fusion at the commissures and fixation of the leaflets. In this instance the valve ring is of normal circumference, but the valve margins are approximated to produce the diminution of the orifice.

Fig. 4.—(Necropsy No. 17,384) Male, fifty-one years. An example of severe stenosis of the mitral valve with the same relationship of orifice to ring as in Fig. 2 but with more marked scarring and rigidity of the cusps. Here, too, the chordae tendineae, although slightly thickened, are not appreciably shortened.

In addition to the 96 specimens with some degree of stenosis, there were 16 specimens showing mitral valvulitis without stenosis (Fig. 7). There was a third group of 7 specimens in which the mitral valve was considered to be anatomically insufficient. In them there was fusion of the commissures with marked retraction of the leaflets and shortening of the chordae tendineae. In some instances adhesion of the posterior

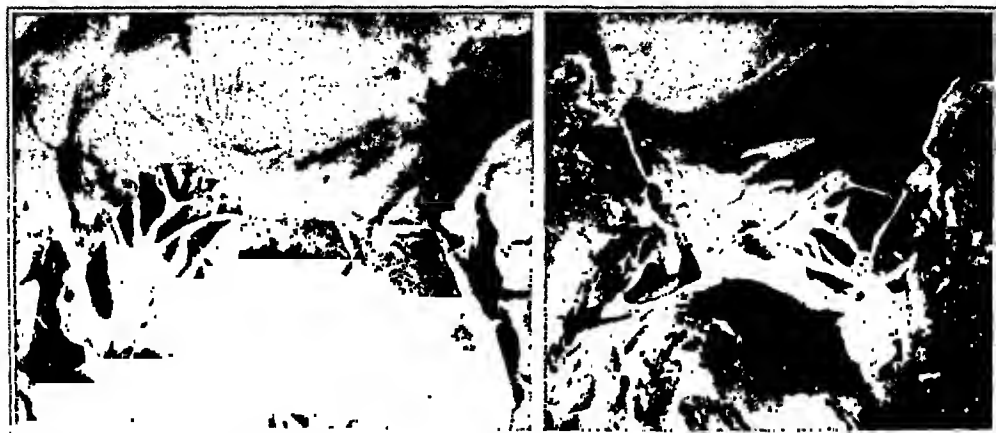


Fig. 5.

Fig. 6.

Figs. 5 and 6.—Mild to moderate atrioventricular valvular stenosis.

Fig. 5.—(Necropsy No. 15,687) Male, seventeen years. This shows mild stenosis of the mitral valve due to thickening of the leaflets at the commissures but with definite retraction of the cusps so that the margin approximates that of the ring. Several chordae tendineae are fused and shortened, and practically all are thickened.

Fig. 6.—(Necropsy No. 17,445) Male, seventy-three years. An example of moderate stenosis of the mitral valve due to cleatrial shortening with fusion of the chordae tendineae. The cusps are only slightly fused at the commissures and only moderately sclerotic.

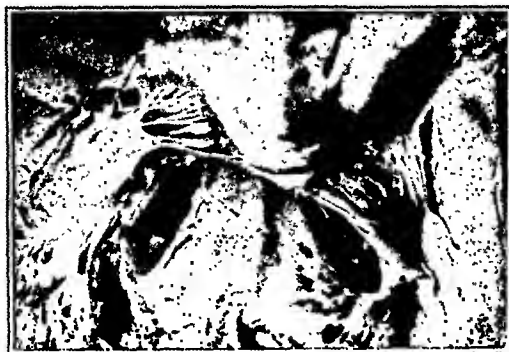


Fig. 7.—Valvulitis without deformity. (Necropsy No. 10,302) Female, fourteen years, who died during first attack of rheumatic fever. The photograph presents verrucous endocarditis of the leaflets of the mitral valve without deformity. Although the valve is somewhat edematous, there is no encroachment on the lumen. Most of the chordae tendineae are normal in length and thickness.

cusps to the adjacent wall was found (Fig. 8). These changes made valvular closure and stenosis impossible. The finding of various grades of auricular dilatation and the presence of endocardial pockets in the wall of the left auricle with apertures facing the valve orifice were accepted as further anatomical evidence of regurgitation.

Ninety-two hearts were available for complete histological study. (Blocks were taken after the standardized procedure of Gross, Antopol and Sacks³² consisting of 10-12, and in most instances 15-18, which included the following sites in the heart: all valves and valve rings, pericardium of the left and right ventricles, left and right auricles, myocardium of the left and right ventricles, the interventricular septum, papillary muscles, base of the aorta and pulmonary artery, the neuromuscular bundle, and the coronary sinns.)

The diagnosis of active rheumatic inflammation³³⁻³⁹ was based on the finding of Aschoff bodies with collagenous necrosis or active valvulitis (nonbacterial), either superficial (verrucous), deep, or both, with or without active pericarditis. Various types of diffuse, nonbacterial valvulitis when associated with varying degrees of myocardial interstitial cellular deposits, especially those adjacent to blood vessels, varying from the Aschoff body to collections of lymphocytes, plasma cells, eosinophiles, polymorphonuclear leucocytes, basophilic mononuclear leucocytes and histiocytes, were also considered positive evidence of active rheumatic inflammation. Recent vascular lesions,^{35, 40-43} particularly in the aorta, pulmonary artery and smaller vessels of other organs, when associated with carditis, were considered evidence of active inflammation. Cases were regarded as inactive (healed) when we found



Fig. 8.—Mitral insufficiency. (Necropsy No. 17,539) Female, twenty-four years. An example of anatomical mitral insufficiency in which there is definite thickening of the valve leaflets with retraction and adhesion of the posterior leaflet to the underlying mural endocardium. The chordae tendineae are only mildly thickened and practically normal in length. The circumference of the valve margin almost equals that of the ring (10 to 10.5 cm.).

(a) A view of the intact mitral orifice as seen from above. The auricle was also markedly dilated.

(b) This view presents the valve after section through the midportion of the posterior leaflet to show the retraction of this cusp in particular and its fusion to the underlying ventricular wall. The arrow points to a pocketlike structure in the endocardium of the left auricle.

perivascular and intrafascicular scarring of the myocardium, scarring and deformity of the valves with vascularization, without microscopic evidence of active inflammation as described, healed pericarditis, healed aortitis, the latter two findings with characteristic lesions elsewhere.

Several of the specimens which appeared to be inactive grossly presented definite evidence histologically of active inflammation, which reemphasizes³⁶⁻³⁸ the need for careful and complete histological studies in deciding on the presence of active rheumatic inflammation. Conversely, what appeared to be verrucae grossly, on histological study proved occasionally to be healed lesions. For this reason the data are analyzed from the standpoint of rheumatic inflammation only in the 92 hearts which were available for histological study.

ANALYSIS OF MATERIAL

First, *what is the relationship of the occurrence of auricular fibrillation to the presence of various grades of mitral stenosis or insufficiency?* About half of each rhythmic group was associated with severe stenosis, and about one-third to one-fourth with mild to moderate stenosis, suggesting that the *rhythm bore no relationship to the grade of stenosis*. It appears that mitral stenosis or organic insufficiency is necessary, however, for the development of *persistent* auricular fibrillation in *rheumatic* heart disease, since there were no cases without significant mitral valvular deformity (Table I).

TABLE I

RHEUMATIC HEARTS. DISTRIBUTION OF CASES ACCORDING TO RHYTHM AND GRADE OF MITRAL VALVE DEFORMITY

MITRAL VALVE DEFORMITY	AURICULAR FIBRILLATION		SINUS RHYTHM		TOTALS	
Severe Stenosis	24	(57%)	38	(49%)	96	(81%)
Mild—Moderate Stenosis	15	(36%)	19	(25%)	7	(6%)
Insufficiency (organic)	3	(7%)	4	(5%)	16	(13%)
None			16	(21%)		
Total	42		77		119	

Second, *what relationship has the occurrence of auricular fibrillation to age at death?* Of 42 hearts from cases of auricular fibrillation, two-thirds were from patients over forty years of age; whereas, of the 77 specimens from cases of sinus rhythm, about one-third was from individuals over forty years of age (Table II). The average age at death, as already stated, was forty-three years in the former. Auricular fibrillation was encountered, therefore, in patients dying with rheumatic heart disease with greater frequency after than under the age of forty. These figures differ somewhat from those given in the clinical studies of Stroud, Laplace and Reisinger²¹ and DeGraff and Lingg.²³ In the former, 35.2 years was the average age at death in rheumatic heart disease with auricular fibrillation; in the latter it was 40 years.

This material differs sharply, however, from that employed clinically. One reason for the difference may be that a rheumatic etiology was not known or even suspected in many cases during life. The clinical studies may be deficient in the number of older individuals, since auricular fibrillation, as is well known, makes the precise diagnosis of mitral stenosis difficult. This series includes patients, furthermore, of all age groups whose death was not caused directly by heart disease.* The clinical studies were limited in all probability to patients treated because they were suffering from heart disease and did not include ambulatory

*Several of the patients died of lobar pneumonia, some of cerebral hemorrhage, others of acute appendicitis, carcinoma of the stomach, carcinoma of the breast, acute and chronic diffuse glomerular nephritis, Henoch's purpura, Graves' disease, sepsis, and fractured skull.

patients unaware of its presence. Cases of bacterial endocarditis were also, as already stated, omitted from this series. In a recent report of Stone and Feil²³ of 100 autopsied cases of severe mitral stenosis, the average age was 40.6 years.

Third, *what relation has the occurrence of auricular fibrillation to the presence and grades of mitral stenosis and insufficiency in the various decades?* When the grades of stenosis in the specimens from the auricular fibrillation group were compared as to frequency under and over

TABLE II

MITRAL VALVE DEFORMITY. CASES ARRANGED ACCORDING TO DEGREE OF DEFORMITY AND AGE IN DECADES

MITRAL VALVE DEFORMITY	CASES OF AURICULAR FIBRILLATION						CASES OF SINUS RHYTHM							
	DECADES						DECADES							
	II	III	IV	V	VI	VII	I	II	III	IV	V	VI	VII	VIII IX
Severe Stenosis	1	4	5	5	6	3		6	7	14	6	3	1	1
Mild—Moderate Stenosis	1	2	1	6	2	3		4	1	2	3	4	4	1
Insufficiency	1	1			1		1	2	1					
Total	3	7	6	11	9	6	1	12	9	16	9	7	5	2
	16			26			38				23			
None	0	0	0	0	0	0	0	5	2	4	2	2	0	1
	Under 40			Over 40			Under 40				Over 40			
Severe	10			14			27				11			
Mild—Moderate	4			11			7				12			
Insufficiency	2			1			4				0			
No stenosis	0			0			11				5			

forty years, stenosis in the younger group was more often severe than mild (10 of 14 specimens, ratio of 2.5:1), while over forty years the incidence approached equality (14 to 11 hearts). In the sinus rhythm group, however, severe stenosis was encountered even more frequently under the age of forty (27 to 7, ratio 4:1), over forty years it was like the fibrillating group (11 to 12, ratio 1:1) (Table II). There is, in short, no relation between the existence of auricular fibrillation and the grade of stenosis in various decades. Most cases of severe stenosis under forty years fall, moreover, in the sinus rhythm group (27 to 10).

Fourth, *what relationship has auricular fibrillation to active rheumatic inflammation independent of the grade of valvular deformity?* Of those cases of auricular fibrillation which were studied microscopically, 17, about half, exhibited some grade of valvular deformity and showed

active inflammation; whereas, of 48 cases of sinus rhythm with some grade of valvular deformity, 30, or three-fifths, presented evidence of active inflammation (Table III).

Evidence of rheumatic inflammation in cases of auricular fibrillation was present in all 12 specimens under the age of forty years, and in 5 of 19, or one-fourth, over the age of forty years. This group is necessarily small, because only those cases were admitted in which a histological study was made. In cases of normal rhythm, evidence of inflammation (activity) was seen in 34 of 41 hearts under forty years and in 8 of the 20 specimens from patients over forty years. It is interesting that of the 12 cases of auricular fibrillation under forty years which were studied histologically, 9 showed active myocarditis, and of these 7 had Aschoff bodies; whereas of the 19 cases over the age of forty years studied histologically only 4 had active myocarditis and of these 2 had the submiliary myocardial nodules. In the sinus rhythm group of 41 cases under forty years, 25 showed active myocarditis and in 21 of these Aschoff bodies were found; while of those over forty years, 5 exhibited active myocarditis and in one there were nodules. These findings suggest that in older subjects active rheumatic inflammation is not a determining factor in the development of auricular fibrillation.

When the grade of severe stenosis in relationship to activity is studied, active inflammation was found in a ratio of 1.4:1 (10 to 7) in the fibrillation group, and in cases of sinus rhythm, in a ratio of 2:1 (20 to 12). In moderate stenosis, activity was found in 5 of 11 specimens from cases of fibrillation and in 6 of 12 of sinus rhythm. Of 53 cases under forty years there were no inactive cases among the fibrillators, whereas in the sinus rhythm group there were 7. Past the age of forty years in both rhythmic groups there were 39 cases, and of these 26 were inactive by the criteria used. This may be interpreted as showing that *under forty years auricular fibrillation may be a manifestation of rheumatic activity in the presence of rheumatic structural cardiac changes in individuals dying in congestive heart failure.*

No special histological features were found differentiating the hearts of the fibrillating from those of the sinus rhythm group. A strict histological comparative examination of the auricles has not been made, however, in this study.

Fifth, *is there any relationship between the occurrence of auricular fibrillation and the presence of cardiac lesions* in addition to mitral valvular deformity?* For the answer to this question the gross material of 119 specimens has been analyzed again (Table IV). In the auricular fibrillation group 57 per cent and in the sinus rhythm group 51 per cent showed significant associated cardiac lesions. Aortic valve deformity occurred more frequently in the sinus rhythm group (30 times against

*The other cardiac lesions, both valvular and pericardial, were examined and classified using the same criteria employed in the study of the mitral valve.

TABLE III
RHEUMATIC ACTIVITY. RELATION TO RHYTHM AND DEGREE OF MITRAL VALVE DEFORMITY ACCORDING TO AGE
(BASED ON HISTOLOGICAL STUDY)

		AURICULAR FIBRILLATION							SINUS RHYTHM							ACTIVITY IN BOTH GROUPS COMBINED	
		II	III	IV	V	VI	VII	I	II	III	IV	V	VI	VII	VIII IX		
Degree of stenosis	DECADE																30
	active	1	4	4	1				6	4	8	2					
	Severe inactive				1	4	2			1	4	3	2	1	1		19
	active	1			4			2				1	1	2			11
	Mild—Moderate inactive				1	2	3				2	1	1	1	1		12
	active	1	1					1	2	1							6
	Mitral insuff. inactive					1											1
	active								4	2	4		1		1		12
	No valve deformity inactive												1				1
	Total	3	5	4	7	7	5	1	14	8	18	7	6	4	3		92
		12							41							20	

31 cases all with defects of mitral valve studied
microscopically.
17 active

48 cases with mitral valve defect studied microscopically.
30 active

13 cases without mitral valve defect studied microscopically.
12 active

14 inactive

18 inactive

17). It is interesting to note that the *relative* incidence in *each rhythmic* group for aortic valve involvement is about the same (40 per cent). The same is true of combined aortic and mitral valve disease. Adherent pericardium occurred more frequently in the sinus rhythm group (14 times against 7).

TABLE IV

DISTRIBUTION OF CASES OF MITRAL VALVE DEFORMITY WITH AND WITHOUT ASSOCIATED CARDIAC LESIONS ACCORDING TO LESION, RHYTHM AND THE PRESENCE OF RHEUMATIC ACTIVITY

CARDIAC LESIONS	AURICULAR FIBRIL- LATION			REGULAR SINUS RHYTHM		
	AC- TIVE*	INAC- TIVE*	TO- TAL†	AC- TIVE*	INAC- TIVE*	TO- TAL†
Mitral and aortic stenosis	4	5	10	13	2	18
Mitral stenosis; aortic insufficiency	1		1	1	1	2
Mitral and tricuspid stenosis	1		2			1
Mitral and tricuspid insufficiency	1		1			
Mitral, aortic, and tricuspid stenosis	1		3	1	1	2
Mitral stenosis; adherent pericardium			3		1	2
Mitral insufficiency; adherent pericardium				3		3
Mitral and aortic stenosis; adherent peri- cardium	1	1	2	3	2	5
Mitral and tricuspid stenosis; adherent peri- cardium	1		1			
Mitral, aortic, and tricuspid insufficiency; adherent pericardium				1		1
Mitral, aortic, and tricuspid stenosis; ad- herent pericardium	1		1			
No mitral valve deformity; adherent peri- cardium				1	1	3
No mitral valve deformity; aortic insuf- ficiency				2		2
Mitral stenosis	5	7	16	8	11	27
Mitral insufficiency	1	1	2			
Mitral valvulitis with no deformity				9		11
Totals	17	14	42	42	19	77

* = Studied histologically.

† = Includes cases studied macroscopically only.

Cases showing organic disease of tricuspid valve (stenosis, insufficiency, or both) were encountered more often in the relatively small auricular fibrillation group than in the much larger sinus rhythm group (8 times against 4).

In the sinus rhythm group the majority of hearts (26 of 39) with multiple lesions appeared below the age of forty years. (Table V.) In the auricular fibrillation group they were, however, evenly divided above and below forty years. Cases were found in both groups late in life. (Table VI.) More active cases with multiple cardiac lesions were found in the sinus rhythm group than among the fibrillators, under the age of forty years. (Table V.) The relative incidence, however, of active cases in each rhythmic group was the same. There was only one case with multiple lesions under forty years which was inactive, and it fell in the sinus rhythm group. In contrast there were 7 inactive among 12 uncom-

plicated cases of mitral stenosis in the sinus rhythm group under the age of forty years. As already stated, *all* the cases under forty years among the fibrillating group were active.

TABLE V

MITRAL VALVE DEFORMITY. COMPARISON OF CASES WITH AND WITHOUT ASSOCIATED CARDIAC LESIONS ACCORDING TO PRESENCE OF RHEUMATIC ACTIVITY, RHYTHM, UNDER AND AFTER AGE 40

		AURICULAR FIBRILLATION		SINUS RHYTHM	
		UNDER 40	AFTER 40	UNDER 40	AFTER 40
Hearts with multiple lesions	Gross cases	12	12	26	13
	*Active	9	2	21	4
	*Inactive	0	6	1	7
Hearts with mitral valve deformity alone	Gross cases	4	14	15	12
	*Active	3	3	5	3
	*Inactive	0	6	7	4

*Includes only cases studied histologically.

TABLE VI

MITRAL VALVE DEFORMITY. DISTRIBUTION IN DECADES OF CASES WITH AND WITHOUT ASSOCIATED CARDIAC LESIONS

AURICULAR FIBRILLATION		DECADES	SINUS RHYTHM	
MITRAL VALVE ALONE	MITRAL VALVE AND ASSOCIATED LESIONS		MITRAL VALVE ALONE	MITRAL VALVE AND ASSOCIATED LESIONS
		1-10		1
	3	10-19	3	11
4	3	20-29	4	5
	6	30-39	8	9
6	5	40-49	4	5
5	4	50-59	3	6
3	3	60-69	4	1
	0	70-80	1	1

Sixth, *to what extent does auricular thrombosis occur in hearts with auricular fibrillation, and is there a relationship to the degree of stenosis and active inflammation?* Thrombi were observed in one or both auricles, or in their appendages in 12 per cent (15 of 119) of all the cases; 10, or 24 per cent, in the auricular fibrillation group, 9 exhibiting signs of active rheumatic inflammation, and 5 in the sinus rhythm group, 3 being active. Combining both groups, 14 of the 15 specimens presented some degree of mitral valvular deformity. Nine showed severe, 5 mild to moderate stenosis, and 1 showed anatomical mitral insufficiency. In the auricular fibrillation group, 6 of the 10 hearts exhibited severe stenosis; in the sinus rhythm group, 3 of the 5 specimens. (Table VII.)

The average age in the auricular fibrillation group with auricular thrombosis was 39.7 years, the extremes being 18 and 52 years; that in the sinus rhythm group was 41.8 years, the extremes 17 and 63. Three-fourths of all the cases occurred in individuals past forty years of age.

Seventh, *what is the mode of death of patients with auricular fibrilla-*

tion, and is there any relationship to the presence of "rheumatic inflammation"? In fibrillation, congestive heart failure was the mode of death in 88 per cent, whereas in sinus rhythm, it was 68 per cent. Approximately half of each group presented histological signs of active rheumatic inflammation. It is of special interest that in the group with auricular fibrillation under the age of forty years all died in congestive heart failure and showed evidence of active rheumatic inflammation.

TABLE VII
AURICULAR THROMBOSIS IN BOTH RHYTHMIC GROUPS

RHYTHM	NO. OF CASES	VALVE DEFORMITY			RHEUMATIC INFLAMMATION	
		SEVERE STENOSIS	MODERATE STENOSIS	INSUFFICIENCY	ACTIVE	INACTIVE
Auricular fibrillation	10	6	3	1	9	1
Regular sinus rhythm	5	3	2	0	3	2

Evidence of active inflammation was found also in all the sinus rhythm cases, with one exception, under forty years dying in congestive failure. The exception was an inactive case with acute heart failure occurring during labor and associated with paroxysmal tachycardia.

The mode of death in the younger patients is undoubtedly referable to the more diffuse involvement of the myocardium by the inflammatory process. As stated in the answer to question 4, active myocarditis and Aschoff bodies are rare findings in the individual past forty years and are all too common in those under this age. The older individuals must, therefore, be suffering from the effects of disease states superimposed on the old rheumatic tissue changes, degenerative changes, or the wearing out effects of long-standing organic defects of the heart, as well as disorders of rhythm.

COMMENT

It becomes apparent from the data presented that a number of factors play a rôle in the development of *persistent* auricular fibrillation in rheumatic heart disease. While the grade of stenosis of the mitral valve orifice was not found to be related to the presence of *established* auricular fibrillation, some degree of valvular deformity appears to be requisite for its appearance (Table I). To reiterate, cases of paroxysmal auricular fibrillation were not included.

In the material studied, patients over 40 years with auricular fibrillation were encountered more frequently (26 against 16) than were those under this age, and more frequently (62 per cent against 36 per cent) than cases of sinus rhythm (Table II). Further, cases with mitral valvular deformity over the age of forty years occurred more frequently in the auricular fibrillation group (26 against 23). These deductions tend to show that age (including the duration of the disease) may play a determining rôle in the development of the abnormal rhythm.

Of particular interest, though the cases are few, is the analysis of the distribution of active cases. All the patients under the age of forty years with auricular fibrillation showed active rheumatic carditis; in contrast, 17 per cent were inactive in the sinus rhythm group. Since all of the active cases in the auricular fibrillation group died with some degree of congestive failure and showed widespread carditis, it may be reaffirmed that active rheumatic inflammation either precipitates congestive failure or by progressive myocardial impairment leads to its development. This is of importance in a consideration of prognosis and the treatment of young patients.

The presence of active rheumatic inflammation in the younger patients with auricular fibrillation may shed some light on the immune processes and the development of subacute bacterial endocarditis. This immunity is apparent and may be due merely to the fact that they are suffering from an antagonistic state, namely, active rheumatic carditis. This explanation does not apply to cases over forty years, since fewer active cases were found past middle life. However, the recent evidence of Saphir and Wile,⁴⁵ a report of cases of subacute *bacterial* endocarditis in children and young adolescents showing coexisting rheumatic tissue changes, indicates need for caution in using anatomical evidence to test an immunological hypothesis.

Directly related to this question is the apparent immunity to bacterial endocarditis of patients with high-grade mitral stenosis. Fulton and Levine²⁷ have already expressed the opinion, similar to that in the preceding paragraph, that this immunity is based on the persistence of a local rheumatic process in the mitral valve which might be antagonistic to the development of bacterial endocarditis. A study of 49 cases of severe mitral stenosis lends support to this view (Table III). The active were to the inactive as 30 is to 19, a ratio of 1.5:1.

No relationship has been found between the two types of relatively immune hearts; that is, those with auricular fibrillation and those with severe mitral stenosis. This point is to be emphasized in view of the opinion expressed by Stone and Feil²⁹ that the rarity of auricular fibrillation in subacute bacterial endocarditis may be explained in part by the rarity of subacute bacterial endocarditis in advanced mitral stenosis, arguing that auricular fibrillation is definitely more common in mitral stenosis, especially in advanced cases. It is to be seen, however, that the incidence of auricular fibrillation in their own selected group of 100 cases of severe mitral stenosis was 53 per cent, and no mention is made concerning the duration of the abnormal rhythm. Further, no distinction is made between the occurrence of auricular fibrillation as a transitory phenomenon in subacute bacterial endocarditis and the development of this disease in patients with the *established* rhythmic disorder.

It is worthy of emphasis that no cases of auricular fibrillation were encountered under the age of forty years without signs of active rheu-

matic inflammation. As a matter of fact, the only case of fibrillation in rheumatic heart disease under forty years *without* activity, which we have studied,²⁸ was one in which bacterial endocarditis developed.

From the point of view of rhythm no significant relationship has been found to exist between the presence of any one or more associated lesions and active rheumatic carditis. One associated lesion appeared to bear a relationship to the rhythm, namely organic disease of the tricuspid valve; it is interesting that of 8 cases with tricuspid involvement which were studied histologically, seven were active.

Mural thrombosis in the material studied was confined to the auricles. It was encountered most often in the fibrillators with severe mitral stenosis and active carditis. Weiss and Davis,⁴⁴ in a study based on an analysis of necropsy protocols of 164 patients dying from rheumatic heart disease, reported organized mural thrombi in 30 cases. Of the 25 in their group in which the rhythm was determined, 22 showed auricular fibrillation. Using a combination of clinical and some pathological criteria, they stated that activity was present in only 18 per cent of their cases with auricular thrombi contrasting with activity of 47 per cent of their entire series of rheumatic hearts. The discrepancy between their results and the analysis presented here may be accounted for by the fact that their pathological data were taken from necropsy protocols and may not have been so comprehensive as the present study from this standpoint.

SUMMARY AND CONCLUSIONS

An analysis based on the study of 119 consecutive rheumatic hearts obtained at necropsy has been correlated with the cardiac rhythm. Correlations have been made with the grade of mitral valvular defect, age, presence of rheumatic inflammation in the heart and blood vessels, associated cardiac lesions, auricular thrombosis, and the mode of death.

It is shown that the occurrence of auricular fibrillation bears no relationship to the grade of mitral stenosis. Stenosis or organic insufficiency of the mitral valve is necessary for the development of *persistent* auricular fibrillation (not the transitory form) in rheumatic heart disease.

Auricular fibrillation in rheumatic heart disease is encountered with greater frequency in persons past middle life.

Auricular fibrillation is a usual manifestation of rheumatic activity in the presence of rheumatic structural cardiac lesions in individuals under forty years of age dying in congestive heart failure.

Significant organic disease of the tricuspid valve associated with mitral valvular disease is found more frequently among patients with auricular fibrillation than in those with sinus rhythm.

Auricular thrombosis in rheumatic heart disease is encountered most frequently in the hearts of individuals with auricular fibrillation, severe mitral stenosis and evidence of active rheumatic inflammation.

The trends seen in the data are discussed in relation to the etiology of the abnormal rhythm in rheumatic cardiac patients and in relation to clinical data concerning the relative immunity of certain types of rheumatic cardiac patients to the development of subacute bacterial endocarditis.

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THE HEARTS OF RICKSHA PULLERS

A STUDY OF THE EFFECT OF CHRONIC EXERTION ON THE CARDIOVASCULAR SYSTEM*

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INTRODUCTION

OUR interest in the effect of prolonged physical exertion on the human cardiovascular system was aroused in 1930, when one of us (C.L.T.), in the course of routine physical examinations, found a markedly enlarged heart in an otherwise healthy ricksha puller employed in one of the departments of the College. This led to the study herein reported.

That physical exercise has an effect on the cardiovascular system has been realized for a great many years, but as to precisely what this effect is, opinions even today are divided. As early as 1628 Harvey¹ in his *Anatomical Studies on the Motion of the Heart and Blood* stated: "So all animals, man included, that have a stronger and more sturdy frame, with large, brawny limbs some distance from the heart, have a more thick, powerful, and muscular heart, as is obvious and necessary. On the contrary, those whose structure is more slender and soft have a more flaccid heart, less massive and weaker, with few or no fibers internally" (referring to the chordae tendineae and papillary muscles). Since the time of Harvey a mass of literature concerning the effect of exercise on the hearts of animals and of men has appeared. For a fairly complete bibliography the reader is referred to *Chronic Effects of Exercise* by Steinhaus² and to *The Physiology of Muscular Exercise* by Bainbridge and others.³

All data derived from studies of animals show that prolonged exertion produces cardiac hypertrophy. Animals in the wild state are known to possess relatively larger heart weight to body weight ratios than their domesticated relatives. The heart of the wild hare, for instance, is three times as heavy, relative to body weight, as that of the tame rabbit. Birds that fly great distances have much larger hearts in comparison with birds that lead a quiet life. Herrmann⁴ demonstrated that heart weight to body weight ratios in racing greyhounds are considerably greater than the figures usually given for dogs. He weighed the hearts of ten thoroughbred greyhounds and found an average of 13.8 grams of heart

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per kilogram of body weight, which is considerably above the average of 7.98 for 200 normal mongrels. While the maximum ratio of the 200 mongrels was 9.98, the most successful runner among his greyhounds had a ratio of 17.3. From studies of the heart weight to body weight ratios of a large number of various animals, both young and full grown, Herrmann concludes that there is some fundamental relationship between the activity of individual mammals and their heart weight, body weight ratio, and that the more sluggish the animal, the smaller is the ratio. Even young greyhounds who have been confined to small kennels have relatively large hearts.⁵

In experimentally controlled studies on animals, Külbs⁶ in 1906, Grober⁷ in 1908, and Thörner⁸ in 1930 all showed that the heart weight to body weight ratios of dogs exercised by running were markedly greater than those of their litter mates who received no exercise. Secher⁹ in 1923 first demonstrated that cardiac hypertrophy experimentally produced by exercise would regress after adequate rest. Twenty-two rats were given daily running exercise for about sixty days, after which all were retired to inactivity. Small groups were then killed at intervals up to seventy-five days. In those killed immediately the heart weight constituted 5 to 6 per cent of the body weight. This percentage decreased until the forty-eighth day, when it reached the normal value of 3.3 to 3.5 per cent. Secher's findings were confirmed and extended by Steinhaus and his coworkers^{10, 11} who studied the effects of running and swimming on the hearts of growing dogs. Four litters consisting of three dogs each were used. One was exercised by running, a second by swimming, while a third served as a control. All the dogs were permitted to play for a brief period twice a day in the open yard. Roentgenograms were secured biweekly throughout the observation, which lasted one and one-half years in most cases. The results were checked by post-mortem findings. The roentgenograms showed that strenuous exercise led to enlargement of heart, beyond that which was accounted for by the growth curve, within three to five weeks after the beginning of exercise. Whenever exercise was discontinued, there was a regression of the heart area in relation to the body weight curve. Autopsy revealed that exercise induced true work hypertrophy of the heart involving both ventricles, with a slight excess in favor of the left side. The enlargement was more marked in swimmers than in runners. There was no indication of comparable hypertrophy of the skeletal musculature of the limbs.

In regard to the effects of exercise on the human cardiovascular system, published findings are not so consistent as those for experimental animals. In explanation Steinhaus² mentions two probable factors: first, the shadow of the heart in man fuses at its lower border with that of the diaphragm; and second, conclusions have been drawn from comparisons of athletes' hearts with a large variety of so-called normal

standards. Two other considerations may be mentioned. First, it is very rare to obtain necropsies of vigorous athletes who meet an accidental death. Second, slight to even moderate hypertrophy may occur during life, but not be particularly obvious even on roentgen-ray examination unless dilatation is also present. As to the immediate effects of strenuous exercise on the size of the heart, Gordon, Levine, and Wilmaers¹² showed it to be reduced immediately upon cessation of exertion, probably because of sudden diminution of venous return to the heart.

There are in general three schools of opinion in regard to the chronic effects of exercise on the cardiovascular system. First, Gordon, Rautmann, and others^{12, 13, 14, 15} hold that the heart size of heavy workers and athletes in general falls within the range for normal individuals of the same size and age. Deutsch and Kauf,¹⁶ who examined several thousand athletes at the Vienna heart station and 32 athletes at the 1928 Amsterdam Olympic Games,¹⁷ hold that the heart shadows of trained athletes average larger than those of similarly built ordinary individuals. According to them enlargement is most noticeable in those long engaged in endurance sports, such as oarsmen, skiers, and cyclists. They interpret this enlargement as dilatation associated with, or brought on by, vagotonia in athletes, since the enlargement usually subsides (though never completely) after several weeks or months of rest, and since bradycardia is such a common finding in athletes.¹⁸ Herxheimer¹⁹ represents the third group who hold that strenuous exercise produces true hypertrophy of the heart. He studied 171 participants in the German games of 1922, 12 professional six-day bicycle racers, and 249 Olympic athletes at Amsterdam in 1928. Eimer's²⁰ investigation of 300 athletes led him in the same direction. Herxheimer²¹ presented the theory that exercises of strength or speed induce hypertrophy of skeletal muscles and only to a small extent of the heart muscle, whereas exercises of endurance cause cardiac hypertrophy without much effect on skeletal muscles. Acker-mann²² measured the hearts of oarsmen before and after a season of training. About half, mostly the younger men, showed definite enlargement at the end of the season.

TWO CASE REPORTS

The following cases are reported as of special interest to the problem.

CASE A.—(No. 43 of the tables). A healthy Chinese male employee of forty-five years, came for routine examination in April, 1930, with negative past and present histories. No cardiovascular or other complaints. Had been pulling a ricksha for about seven years, with an average of about four hours' actual running per day. Well developed and fairly well nourished. The only positive findings were moderate cardiac enlargement to the left and a slow heart rate, 48 per minute. Heart sounds of good quality. No murmurs. No detectable arteriosclerosis. No edema. Blood pressure 89 mm. Hg systolic and 62 mm. diastolic. Urine normal. Blood Wassermann reaction negative. A teleroentgenogram of the heart

(Fig. 1) showed a cardiac area on the frontal plane of 151.6 sq. cm., 47 sq. cm. above the estimated normal value for his height and weight. The cardiothoracic ratio of Danzer was 0.56. Although the man had no symptoms or signs pointing to cardiac insufficiency, it was thought that he should give up ricksha pulling. He was consequently transferred to an indoor occupation which necessitated no significant physical activity.

Further examination in April, 1933, three years after cessation of ricksha pulling, showed that the individual was in good physical condition. His heart was still enlarged to the left, though it appeared to be smaller than it had been three years before. The teleroentgenogram (Fig. 2) taken with the same technic showed a frontal heart area of 127.7 sq. cm., 23 sq. cm. oversized, but smaller than in 1930 by about 24 sq. cm. From the roentgenographic appearance, although the heart as a whole was reduced in size, the decrease involved chiefly the left ventricle. Electrocardiograms taken in 1930 and in 1933 revealed nothing remarkable.

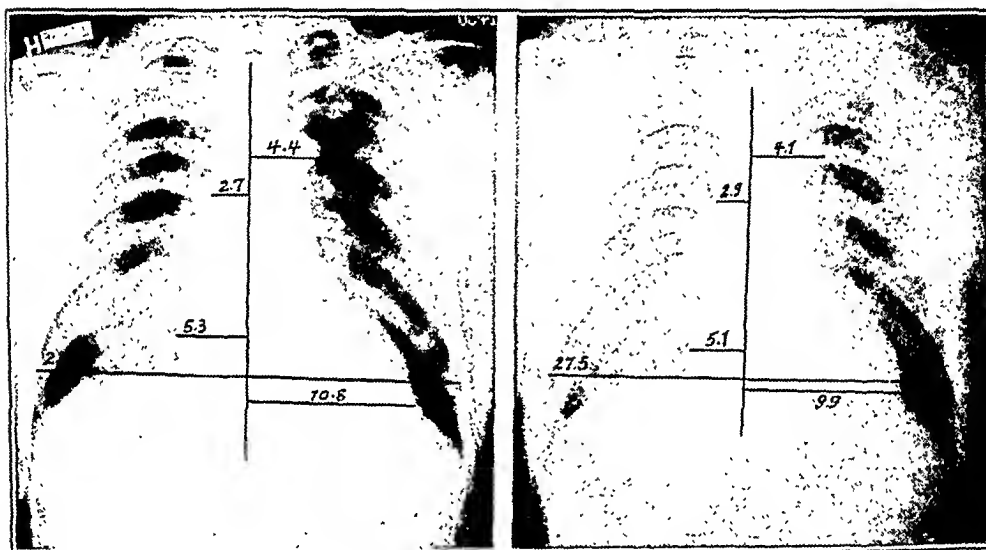


Fig. 1.

Fig. 2.

Fig. 1.—Case 43a. Ricksha puller for seven years. April 13, 1930. Estimated cardiac area 104.65 sq. cm. Measured area 151.60 sq. cm. Heart oversize 47 sq. cm., or 45 per cent. Cardiothoracic ratio 0.56.

Fig. 2.—Case 43b. April 25, 1933, after three years of inactive occupation. Estimated cardiac area 104.84 sq. cm. Measured area 127.70 sq. cm. Heart oversize 22.86 sq. cm., or 22 per cent. Cardiothoracic ratio 0.54.

CASE B.—(Hosp. No. 40,272, not included in the group studied). A Chinese man, aged forty-seven years, admitted to the Surgical Service for anal fistula of twenty-nine years' duration. No complaint, except for the local condition. No symptom referable to the pulmonary or cardiovascular system. Venereal exposure denied; no intravenous medication. X-ray examination of the chest for tuberculosis revealed no evidence of tuberculosis, but a moderately enlarged heart, involving especially the left ventricle, both in frontal view and in left anterior oblique view, and marked enlargement or bulging of the ascending portion of the aortic arch (Fig. 3). Estimated cardiac area 98.94 sq. cm. and measured area 133.90 sq. cm., an increase of 35 sq. cm. Cardio-thoracic ratio 0.59. Diameter of the aortic shadow 8.2 cm.

Examination by the medical consultant showed no dyspnea or cyanosis. Faint pulsation in the right third interspace, but no thrill felt. Precordial impulse felt in the fifth and sixth intercostal spaces, 3 cm. beyond the midclavicular line. There was retromanubrial dullness and also dullness extending about 4 cm. to the right

of the midsternum in the second, third, and fourth intercostal spaces. Heart sounds of good quality; no accentuation or change in the quality of the aortic second sound. No murmur. Heart rate about 57, rhythm regular. Blood pressure 128 mm. Hg systolic and 72 mm. diastolic. No evidence of peripheral arteriosclerosis; no congestion of any viscera; no peripheral edema. No anemia or polycythemia. Urine normal. Ocular fundi showed slightly tortuous veins, normal in size; arteries apparently slightly narrower than usual; mild Gunn's crossing signs. These findings impressed the examiner as suggesting early primary hypertension. Both blood Wassermann and Kahn reactions negative on three occasions, about a month apart. Spinal fluid entirely normal, with flat colloidal gold and gum mastic curves and negative Wassermann reaction. Electrocardiogram showed sino-auricular rhythm, rate 57, auriculoventricular conduction time 0.21 second.

On inquiry it was found that the patient had been an active ricksha puller for eighteen years, with an average of about four hours' actual running per day. How-

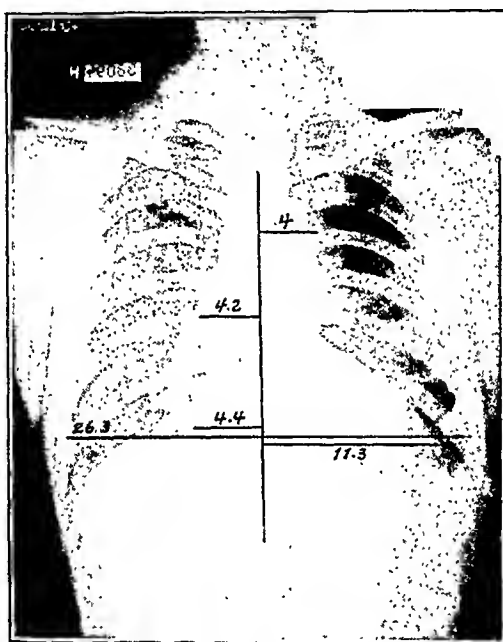


Fig. 3.—Case B (see case reports; not in the tables). Ricksha puller for eighteen years. Estimated cardiac area 98.94 sq. cm. Measured area 133.90 sq. cm. Heart over-size 35 sq. cm., or 35 per cent. Cardiothoracic ratio 0.59. Note the bulging of the ascending portion of the aortic arch.

ever, he insisted that he had always been in excellent health except for the anal fistula. Although it is possible that this patient may have syphilitic cardiovascular disease, it is extremely unlikely. It seems that the aortic dilatation and cardiac enlargement may well be the result of the patient's life as a ricksha puller.

MATERIAL AND METHODS

In an effort to throw further light on the problem of the effects of prolonged exertion on the heart, we have studied 46 ricksha pullers (all male). For the sake of those who have not seen a ricksha in use, it may be stated that it is a rather light narrow carriage, with two wire-spoked, rubber-tired wheels; a seat is mounted on leafed springs over the axle. The wheels are ball-bearing. Two shafts connected at the front by a

cross-piece extend forward. It is pulled by an individual who stands between the shafts. No effort is required to hold up the shaft, because once raised the rider and seat are balanced over the axle. On level ground little energy is needed to maintain the pull on the ricksha, and the energy is chiefly consumed in running, which at one stretch may vary from a short distance to one or two miles.

Most of the group of ricksha pullers studied are privately employed by members of the staff of the College. All the subjects had been ricksha pullers for at least one year. Their living conditions are fairly good. They usually have adequate rest between periods of activity. All of them were physically healthy and free from cardiovascular and other systemic disease. None of them was anemic. There was no evidence of nephritis in any. None of the group had any undue dyspnea after moderate speed and duration of pulling. There was no cyanosis or edema in any of them. None showed a cardiac diastolic murmur. The Wassermann test was not performed as a routine; some of the subjects had a previous record of a negative test. One of them (No. 33) had a positive blood Wassermann with no manifest syphilitic lesion. In short, all were athletic and apparently healthy individuals.

Groups of four or more subjects were examined by two of us (C.L.T. and C.W.B.) in the afternoon. All were given adequate rest before the examination. Quite a number came rather reluctantly, and a few were excited and almost refused the examination. Such an emotional upset may account for the tachycardia and slight elevation of blood pressure (which usually disappeared after reassurance) noted in a number of cases. The physical examination was carried out before roentgenologic and electrocardiographic studies were made. Particular attention was paid to the cardiovascular system, although it must be stated that only a brief period was available for physical examination in order that all studies could be completed in one afternoon. During the physical examination the heart was considered "not enlarged" when the outermost point at which a distinct cardiac impulse could be felt was on or within the midclavicular line, or the outermost point of the cardiac dullness on light percussion was on or within the same line. The heart was considered "enlarged" when the cardiac impulse could be distinctly felt beyond the midclavicular line, or if this was not palpable, when the relative cardiac dullness extended beyond that line. Determination of the cardiac size by physical examination is subject to error from at least three factors, aside from the error due to haste in the examination or to poor technique. When the heart is hyperactive, as in excitement and apprehension, the vibration of the precordial region may be so widespread that the heart may be considered enlarged, while actually it is not. Even when the left border of the heart is beyond the midclavicular line, decision as to the size of the heart is fraught with insecurity if the measured cardiac area in the teleroentgenogram is not above the upper

limit of the estimated normal. On the other hand, when enlargement of the heart is general or more right-sided, the left border may be within the midclavicular line, while the heart is actually oversize.

Blood pressure was taken by the auscultatory method, and the beginning of the fourth phase was taken as the diastolic level. The peripheral arteries were considered "thickened" when the wall of either the brachial or radial artery or both, emptied of its blood content, could be readily felt by the palpating finger. Complete urinalysis was done. The finding of a trace of albumin and leucocytes in the sediment could usually be traced to chronic gonococcal urethritis.

The final decision as to whether the heart was enlarged or not was based on the results of radiological study. At the laboratory the subject was first examined under the fluoroscope in various positions. Particular attention was paid to the heart and the aortic arch. A frontal teleroentgenogram with the subject at a distance of two meters from the target was then taken. An additional film was taken with the subject in the left anterior oblique position, facing the film at an angle of 45 degrees. In the latter position the two ventricles can be better visualized and their relative size determined more accurately after the method originally suggested by Fray.²³ The cardiac area was measured with a planimeter. The difference between the measured area and the estimated normal area was recorded and then expressed in percentage. The estimation of cardiac area was done according to the method of Hodges and Eyster.²⁴ In addition the cardiothoracic ratio of Danzer²⁵ was calculated.

With the string standardized so that a current of one millivolt gave a deflection of one centimeter on the record, Leads I, II, and III of the electrocardiogram were taken from each subject in the recumbent position. The subjects were not in a basal condition. The T-wave was considered tall in a lead when its height was above 5 mm. The presence of right or left "axis deviation" was determined from Leads I and III. The longest P-R interval was measured, usually in Lead II. The R-R interval and the Q-T interval were determined by taking the average values of four cycles. The relative duration of electrical systole as expressed in the formula, K equals the Q-T interval divided by the square root of the R-R interval, was then calculated.²⁶

RESULTS

Table I summarizes the results of the physical findings in these 46 ricksha pullers. Their mean age was thirty-three years. The period during which they had been engaged in their occupation averaged about eight years. The extremes were one year and twenty-five years. Most of the subjects actually pulled from two to four hours per day (mean, 3.3 hours). Twenty-one of the 46 subjects (45 per cent) revealed evidence of cardiac enlargement. Thickening of brachial or radial artery

TABLE I
PHYSICAL FINDINGS IN 46 RICKSHA PULLERS (All Male)

NO.	AGE	ACTIV- ITY	AC- TUAL PULL- ING PER DAY	HEART SIZE	PERIPH- ERAL ARTERIES	BLOOD PRESSURE	CARDIAC MURMURS	URINE
	Years	Years	Hours			mm. Hg		
1	19	2	4	Not enlarged	Soft	100/68	Systolic apical	Normal
2	21	6	3	Not enlarged	Soft	90/56	None	Normal
3*	22	2	3	Not enlarged	Soft	92/64	None	Normal
4	22	2	3	Not enlarged	Thickened	120/82	None	Normal
5	22	3	2	Enlarged	Soft	106/72	None	Normal
6	24	3	4	Not enlarged	Soft	116/78	None	Normal
7	24	1	1	Not enlarged	Soft	106/70	None	Normal
8	25	2	3	Enlarged	Soft	100/60	None	Trace albu- min, many W.B.C.
9*	26	3	4	Not enlarged	Soft	116/46	Systolic apical and basal	Normal
10	27	7	4	Enlarged	Soft	134/90	None	Normal
11*	27	2	3	Enlarged	Soft	128/80	Systolic basal	Normal
12	28	5	3	Not enlarged	Thickened	102/80	None	Trace albu- min, many W.B.C.
13*	29	15	3	Not enlarged	Thickened	130/90	None	Normal
14*	29	8	2	Enlarged	Soft	124/68	None	Normal
15*	30	7	3	Not enlarged	Soft	104/62	None	Normal
16	30	7	4	Enlarged	Soft	96/66	None	Normal
17	30	12	4	Not enlarged	Soft	112/76	None	Trace albu- min, many W.B.C.
18*	30	4	2	Enlarged	Soft	116/76	None	Normal
19*	30	9	3	Enlarged	Thickened	120/74	Systolic apical	Normal
20*	31	2	6	Not enlarged	Soft	134/78	Systolic apical and basal	Normal
21	31	2	3	Not enlarged	Soft	108/80	None	Normal
22*	32	10	4	Enlarged	Soft	126/78	None	Normal
23*	33	5	3	Not enlarged	Soft	112/84	None	Normal
24a	31	10	2	Enlarged	Thickened	118/82	None	Normal
24b	33	12	2	Enlarged	Thickened	110/68	None	Normal
25	35	10	2	Not enlarged	Thickened	126/80	None	Normal

*Cases so marked have cardiac areas 15 per cent or more above the estimated area in teleroentgenograms. In the calculation of mean values, 24a, 32a, 43b, and 45a were excluded. The records of 43b were obtained after three years of an inactive occupation.

TABLE I—CONT'D

NO.	AGE	ACTIV- ITY	AC- TUAL PULL- ING PER DAY	HEART SIZE	PERIPH- ERAL ARTERIES	BLOOD PRESSURE	CARDIAC MURMURS	URINE
	<i>Years</i>	<i>Years</i>	<i>Hours</i>			<i>mm. Hg</i>		
26*	35	6	4	Enlarged	Thickened	126/88	None	Normal
27*	35	4	4	Not enlarged	Soft	110/80	None	Normal
28	36	7	3	Enlarged	Thickened	134/84	None	Normal
29	36	10	3	Not enlarged	Soft	116/80	None	Normal
30	36	15	2	Enlarged	Soft	134/84	Systolic basal	Normal
31*	36	12	6	Enlarged	Soft	120/86	None	Normal
32a	35	4	5	Not enlarged	Thickened	108/72	None	Normal
32b	37	6	5	Not enlarged	Thickened	114/76	None	Normal
33	37	6	4	Not enlarged	Soft	108/72	None	Normal
34	38	20	2	Enlarged	Sclerotic and tortuous	108/78	Systolic apical	Normal
35	39	13	3	Enlarged	Soft	128/72	Systolic apical	Normal
36	39	14	2	Not enlarged	Soft	122/80	Systolic basal	Normal
37	40	25	3	Not enlarged	Soft	104/74	None	Normal
38	40	20	3	Not enlarged	Soft	104/70	None	Normal
39*	40	18	3	Not enlarged	Sclerotic	120/80	None	Trace albu- min, many W.B.C.
40*	41	10	3	Not enlarged	Soft	108/78	None	Normal
41*	42	10	3	Enlarged	Thickened	120/80	None	Trace albu- min, few W.B.C.
42	44	7	3	Enlarged	Sclerotic	112/80	Systolic apical	Trace albu- min, occa- sional granular casts
43a*	45	7	4	Enlarged	Soft	80/48	None	Normal
43b*	48	—	—	Enlarged	Soft	88/60	None	Normal
44*	47	5	4	Enlarged	Sclerotic	104/70	Systolic apical and basal	Normal
45a	47	15	5	Not enlarged	Soft	96/64	None	Normal
45b	49	17	5	Not enlarged	Soft	106/76	None	Normal
46*	49	18	6	Enlarged	Thickened	116/76	None	Normal
Mean	33	8	3.3			114/75		

was noted in 17 individuals; the brachial artery was sclerotic and tortuous in one man who was thirty-four years of age. These findings are suggestive of early arteriosclerosis. It is our impression that there is a

TABLE II
TELEOROENTGENOGRAPHIC FINDINGS IN 46 RICKSHA PULLERS

TABLE II TELEORONTGENOGRAPHIC FINDINGS IN 46 RICKSHA PULLERS														AMERICAN HEART JOURNAL
NO.	HEIGHT		WEIGHT	ESTIMATED CARDIAC AREA		MEASURED CARDIAC AREA		DIFFERENCE <i>per cent</i>	CARDIO- THORACIC RATIO	AORTIC DIAMETER		ROENTGENOLOGICAL IMPRESSION		
	cm.	kg.		sq. cm.	sq. cm.	cm.								
1	157.0	47.0	88.77	97.24	96.20	- 5	12.0:24.2 0.50	5.2	Normal heart					
2	166.0	54.0	104.18	107.54	125.70	- 1	12.7:23.5 0.54	4.4	Normal heart. Slight left ventricular en- largement					
3*	171.0	56.5	107.54	103.80	114.40	+21	13.9:27.6 0.50	6.5	General cardiac enlargement					
4	174.0	58.7	103.80	106.05	112.40	+ 6	13.2:26.0 0.51	7.0	Normal heart. Aortic shadow slightly wid- ened					
5	169.0	60.5	102.34	115.20	110.30	+ 8	13.3:25.5 0.52	5.8	Normal heart					
6	175.5	50.5	88.77	93.80	115.20	+ 4	13.3:25.4 0.52	5.7	Normal heart. Slight left ventricular en- largement					
7	168.0	57.5	100.07	116.20	93.80	+ 7	12.9:27.5 0.47	5.6	Slight cardiac enlargement					
8	154.5	51.0	98.41	111.00	116.20	+16	13.4:23.6 0.57	5.7	Left ventricular enlargement					
9*	165.5	58.5				+13	13.7:26.0 0.53	6.5	General cardiac enlargement					
10	164.0	60.4					13.9:24.5 0.56	6.5	General cardiac enlargement					

TABLE II—CONT'D

NO.	HEIGHT	WEIGHT	ESTIMATED CARDIAC AREA	MEASURED CARDIAC AREA	DIFFERENCE	CARDIO- THORACIC RATIO	AORTIC DIAMETER	ROENTGENOLOGICAL IMPRESSION
	cm.	kg.	sq. cm.	sq. cm.	per cent		cm.	
11*	164.0	52.2	96.63	128.80	+35	13.5:25.0 0.54	5.8	Left ventricular cardiac enlargement
12	160.0	51.3	92.84	90.50	- 2	11.2:27.0 0.41	5.8	Normal heart
13*	171.5	63.3	106.92	126.20	+18	14.4:26.7 0.53	8.0	General cardiac enlargement. Aortic arch widened and slightly tortuous
14*	168.0	52.4	100.18	136.30	+36	13.1:24.0 0.54	5.8	General cardiac enlargement
15*	172.0	60.0	106.24	122.00	+15	14.6:25.0 0.58	5.6	Left ventricular cardiac enlargement
16	168.0	53.0	100.38	97.75	- 3	13.0:26.0 0.50	5.1	Normal heart
17	180.0	61.3	113.64	92.70	-10	12.4:26.5 0.47	6.0	Normal heart. Aortic arch elongated
18*	166.0	58.0	100.34	124.20	+24	13.5:29.0 0.47	5.7	General cardiac enlargement
19*	166.0	53.0	98.64	115.00	+16	13.7:25.5 0.54	6.1	Left ventricular cardiac enlargement
20*	160.0	54.8	94.03	123.40	+31	13.5:25.6 0.53	6.4	General cardiac enlargement

TABLE II—CONT'D

NO.	HEIGHT cm.	WEIGHT kg.	ESTIMATED CARDIAC AREA sq. cm.	MEASURED CARDIAC AREA sq. cm.	DIFFERENCE		CARDIO- THORACIC RATIO	AORTIC DIAMETER cm.	ROENTGENOLOGICAL IMPRESSION
					per cent	+ 2			
21	160.0	53.7	101.50	103.80			12.7:24.8 0.51	5.7	Normal heart
22*	166.0	56.5	99.83	136.90		+37	14.6:25.0 0.58	7.1	Left ventricular cardiac enlargement
23*	160.4	62.6	97.03	144.60		+49	15.0:25.0 0.60	7.0	Marked general cardiac enlargement ventricle prominent
24a	190.0	75.0	127.00	112.00		-13	13.5:26.6 0.51	5.7	Normal heart
24b	192.0	76.0	129.25	123.35		-5	13.8:26.7 0.52	5.5	Normal heart
25	177.0	63.8	111.88	119.10		+6	14.4:28.8 0.50	7.5	Normal heart. Aortic shadow widened
26*	156.0	56.2	91.03	137.30		+51	14.4:27.8 0.52	7.6	Marked general cardiac enlargement. Aortic shadow widened
27*	167.0	103.66	123.60	123.60		+19	14.5:28.5 0.50	6.8	General cardiac enlargement
28	172.0	111.05	125.40	125.40		+14	14.5:29.0 0.50	6.8	General cardiac enlargement
29	182.0	116.06	111.70	111.70		-4	13.6:24.0 0.57	5.9	Normal heart. Left ventricle prominent

TABLE II—CONT'D

NO.	HEIGHT	WEIGHT	ESTIMATED CARDIAC AREA	MEASURED CARDIAC AREA	DIFFERENCE	CARDIO- THORACIC RATIO	AORTIC DIAMETER	ROENTGENOLOGICAL IMPRESSION
	cm.	kg.	sq. cm.	sq. cm.	per cent		cm.	
30	157.0	55.2	91.55	98.50	+ 8	13.3:25.5 0.52	5.5	Normal heart
31*	168.0	61.0	103.10	120.80	+17	13.3:28.0 0.48	5.5	Left ventricular cardiac enlargement
32a	162.0	54.0	95.57	103.00	+ 7	12.8:26.5 0.48	5.9	Normal heart
32b	162.0	54.0	95.57	91.85	- 4	12.2:29.5 0.42	5.4	Normal heart
33	174.5	57.6	108.60	113.65	+ 4	13.5:29.5 0.46	5.3	Normal heart
34	171.3	66.0	107.67	113.60	+ 6	13.4:26.5 0.51	6.4	Normal heart. Aortic arch tortuous
35	168.5	57.5	102.34	115.20	+13	12.9:27.5 0.47	5.6	Left ventricular cardiac enlargement
36	169.5	61.3	104.50	103.90	- 1	11.7:29.0 0.40	5.5	Normal heart
37	168.5	53.3	100.91	88.80	-12	12.2:24.0 0.51	5.8	Normal heart
38	172.0	60.0	106.14	106.10	0	13.2:26.5 0.50	7.0	Normal heart. Aortic arch tortuous and elongated

TABLE II—CONT'D

NO.	HEIGHT cm.	WEIGHT kg.	ESTIMATED		MEASURED		DIFFERENCE per cent	CARDIO- THORACIC RATIO	AORTIC DIAMETER cm.	ROENTGENOLOGICAL IMPRESSION
			CARDIAC AREA sq. cm.	CARDIAC AREA sq. cm.	CARDIAC AREA sq. cm.	CARDIAC AREA sq. cm.				
39*	174.5	63.0	109.43	109.43	129.30	129.30	+18	13.3:28.0 0.48	7.9	General cardiac enlargement. Aortic arch prominent and elongated
40*	164.5	57.3	98.80	98.80	120.80	120.80	+22	15.0:25.0 0.60	6.3	Left ventricular cardiac enlargement
41*	175.0	58.0	108.14	108.14	141.50	141.50	+31	15.4:27.0 0.57	6.7	General cardiac enlargement
42	156.0	41.7	86.10	86.10	90.00	90.00	+5	11.1:23.2 0.47	5.4	Normal heart. Aortic arch tortuous
43a*	169.0	63.0	104.65	104.65	151.60	151.60	+45	16.1:28.3 0.56	7.1	Marked cardiac enlargement, especially of left ventricle
43b*	170.0	61.0	104.84	104.84	127.70	127.70	+22	15.0:27.5 0.54	7.0	Heart still enlarged, but smaller. Reduction in left ventricle chiefly
44*	160.5	52.7	93.74	93.74	116.80	116.80	+25	13.9:26.0 0.52	6.1	Left ventricular cardiac enlargement
45a	178.0	63.4	112.65	112.65	109.00	109.00	-3	13.2:26.2 0.50	6.4	Normal heart
45b	178.0	63.5	112.65	112.65	106.30	106.30	-6	13.7:29.7 0.47	5.7	Normal heart. Aortic arch elongated
46*	152.0	41.0	82.38	82.38	102.33	102.33	+24	13.6:25.8 0.49	6.5	Left ventricular cardiac enlargement
Mean	167.8	57.6	103.5 ± 2.6	103.5 ± 2.6	114.6 ± 2.3	114.6 ± 2.3	+13.2 ± 2.3	0.51	6.1	

*Cases so marked have cardiac areas 15 per cent or more above the estimated area. In the calculation of the mean values, 21a, 32a, 43b, and 45a, were excluded.

higher incidence of the thickening of the peripheral arteries in this group than is usually found in physical examinations of healthy individuals of the same age periods.

The mean blood pressure was 114 mm. Hg systolic and 75 mm. diastolic; the mean pulse pressure was 39 mm. The pressure tended to be high in a few cases. Blood pressures of 130 mm. systolic and 90 mm. diastolic in a young man of twenty-nine years (Case 13) and of 134 mm. systolic and 84 mm. diastolic in two subjects thirty-six years old (Cases 28 and 30) are not usual among the Northern Chinese. The mean values are very slightly higher than the mean and median systolic pressure of 107 and diastolic pressure of 70 in a series of 342 healthy, active Northern Chinese males of the age period of thirty to thirty-nine years.²⁷

The roentgenological findings are summarized in Table II. The results of the fluoroscopic examination are incorporated in the column, "General impression," which represents the opinion of one of us, the roentgenologist (C.K.H.). In evaluating the measured frontal cardiac areas in teleroentgenograms, the tables of Hodges and Eyster²⁴ for the calculation of the expected normal area have been used. These tables are based on a study of 70 normal Americans. Whether they apply strictly to Chinese subjects has not been definitely settled, but our measurements of the cardiac area of 140 normal, healthy, adult Chinese

TABLE III

PERCENTAGE DEVIATION FROM CARDIAC AREA ESTIMATED FROM HEIGHT AND WEIGHT

PERCENTAGE DEVIATION FROM ESTIMATED CARDIAC AREA	NORMAL CHINESE MALES		RICKSHA PULLERS	
	NUMBER	PER CENT	NUMBER	PER CENT
-30 to -26	1	1.0	0	0
-25 to -16	8	6.0	0	0
-15 to - 6	55	39.0	3	6.5
	==	==	12	26.0
- 5 to + 4	56	40.0	==	==
	==	==	11	24.0
+ 5 to +14	17	12.0	==	==
	==	==	11	24.0
+15 to +24	3	2.0	==	==
+25 to +34	0	0	3	6.5
+35 to +44	0	0	3	6.5
+45 to +54	0	0	3	6.5
Total	140	100	46	100

males, mostly staff members and medical students of this institution, show that the mean cardiac area of normal Chinese males is 4.2 per cent (± 0.68 standard error) smaller than that predicted from age, height, and weight. In Table III it will be seen that 79 per cent of normal Chinese males have measured cardiac area between -15 per cent and +4 per cent and only 12 per cent between +5 and +14 per cent. Thus the cardiac area of normal Chinese males tends to be undersized by about 4 per cent, when compared with predicted area calculated according to

Fig. 4.



Fig. 5.



Fig. 6.

Fig. 7.

- Fig. 4.—Case 26. Ricksha puller for six years. Estimated cardiac area 91.03 sq. cm. Measured area 137.30 sq. cm. Heart oversize 46.27 sq. cm., or 51 per cent. Cardiothoracic ratio 0.52.
- Fig. 5.—Case 41. Ricksha puller for ten years. Estimated cardiac area 108.14 sq. cm. Measured area 141.50 sq. cm. Heart oversize 33.36 sq. cm., or 31 per cent. Cardiothoracic ratio 0.57.
- Fig. 6.—Case 23. Ricksha puller for five years. Estimated cardiac area 97.03 sq. cm. Measured area 144.60 sq. cm. Heart oversize 47.57 sq. cm., or 49 per cent. Cardiothoracic ratio 0.60.
- Fig. 7.—Case 27. Ricksha puller for four years. Estimated cardiac area 103.66 sq. cm. Measured area 123.60 sq. cm. Heart oversize 19.94 sq. cm., or 19 per cent. Cardiothoracic ratio 0.50.

Hodges' method. These results seem to justify fully the use of the tables referred to.

In Cases 23, 32, and 45 there were two examinations done two years apart, and in Case 43 the first examination was done when the subject was engaged in ricksha pulling and the other after he had been in a sedentary occupation for three years. In the final calculation of the data the results of the more recent examination, when the subject had more than one, were included as representative, with the exception of Case 43, as the result of the later examination was considered to be affected by the three years' rest.

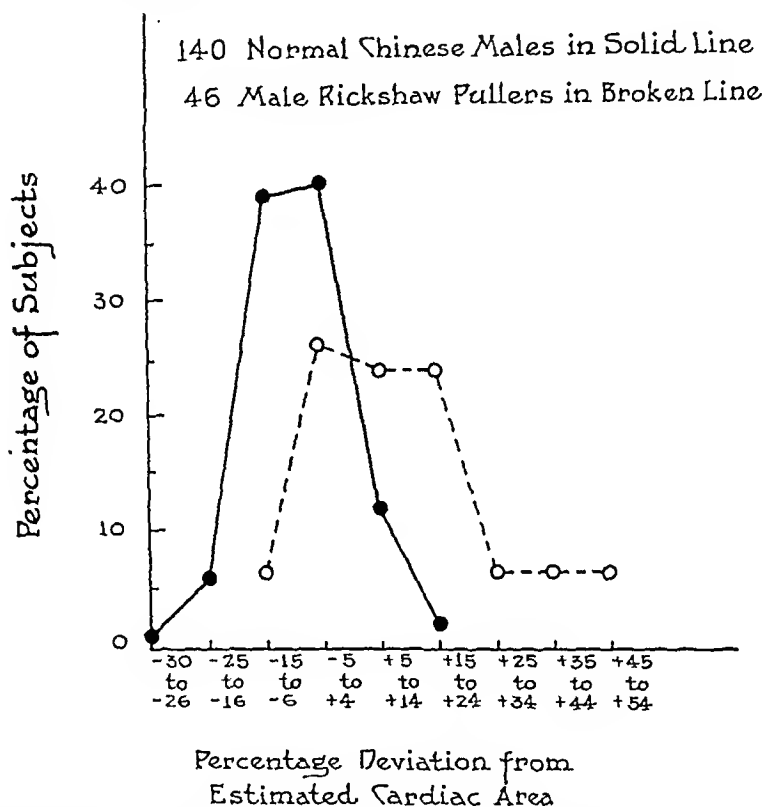


Fig. 8.—Distribution curves comparing the cardiac areas of 46 rickshaw pullers (males) and those of 140 normal Chinese men. For each subject the difference between the measured area and the estimated area is expressed in per cent.

According to Hodges and Eyster, with an observed area 14 sq. cm. larger than the predicted area, the chances are ten to one that the heart is abnormally large. On this basis, which is also in accord with our clinical experience, we have considered a heart to be definitely enlarged when the observed area is 15 per cent or more above the predicted area, since we think percentage deviation is more significant than the difference in actual square centimeters. Of the 46 subjects, 20, or 43 per cent, had observed heart areas larger than the predicted area by 15 per cent or more.

Figs. 1, 2, 4, 5, 6, 7, 8 are examples of x-ray shadows of enlarged hearts.

We may compare our findings in ricksha pullers with the results in the group of 140 normal adult male Chinese by referring to Table III and Fig. 8. Statistically the data may be summarized as follows:

DEVIATION OF CARDIAC AREA	MEAN VALUE \pm STANDARD ERROR
46 ricksha pullers	$+ 13.2 \pm 2.3$ per cent
140 normal adult male Chinese	$- 4.2 \pm 0.68$ per cent
Difference	17.4 ± 2.38

The results for the 46 ricksha pullers in comparison with the American standard are shown below:

Average measured cardiac area	114.6 ± 2.3 sq. cm.
Average estimated cardiac area	103.5 ± 2.6 sq. cm.
Difference	11.1 ± 3.5 sq. cm.

The differences, especially that between the mean deviation of the cardiac area of ricksha pullers and that of the cardiac area of normal Chinese, are clearly statistically significant.

In order to evaluate the cardiothoracic ratio of Danzer,²⁵ a study was made of 116 of the 140 telecardiograms of normal male Chinese. The resulting mean ratio is 0.485 ± 0.004 (standard error). It would seem safe to assume that a ratio of 0.52 or more indicates some degree of cardiac enlargement. In Tables II and III it is shown that the ratio is 0.52 or greater in 22 (48 per cent) of the 46 ricksha pullers. This slightly higher percentage of cardiac enlargement than was shown by the measured area is probably due to the fact that while cardiac enlargement is usually general in nature, there is a tendency to a preponderant enlargement of the left ventricle, as may be seen in Figs. 1, 2, 4, 5, 6, 7.

In summary, nearly half of the ricksha pullers examined showed demonstrable cardiac enlargement (43 to 48 per cent according to the criterion used). Conversely over half the subjects showed no evidence of enlargement beyond the normal limit.

Examination of the data fails to disclose any relation between the years of activity, (minimum, one year) and the occurrence of enlargement of the heart, which was present in four men who had pulled for only two or three years (Cases 3, 9, 11, and 20) and absent in eleven who had been in this occupation for ten or more years (Cases 17, 24, 25, 29, 30, 34, 35, 36, 37, 38, 45).

ACTIVITY	HEART NORMAL	HEART ENLARGED	TOTAL
1 to 4 years	7	6	13
5 to 9 years	8	7	15
10 or more years	11	7	18
Total	26	20	46

In addition to its size, the shape of the heart shadow of ricksha pullers needs brief mention. Although general cardiac enlargement was the usual finding, at least slight left ventricular enlargement was noted

in 15 instances, both among those that showed demonstrable total cardiac enlargement and among those that did not. The diameter of the aortic shadow measured 7 cm. or more in nine subjects. The aortic arch appeared to be elongated or tortuous, or both, in seven instances. Such findings are not usually encountered in healthy subjects of the same age period.

The electrocardiographic findings are not of great interest. The heart rate was not basal as the subjects were examined under the ordinary conditions in the laboratory. It may, therefore, be noteworthy that seven subjects had a rate below 60 beats per minute, and that the average rate was only 68. The electrical axis of the QRS complex lay within normal limits in 40 subjects; in one there was right axis deviation and in five left axis deviation. One striking feature is that in 16 cases the T deflection was tall in one or more leads.

The auriculoventricular conduction time was 0.20 second in eight individuals and beyond 0.20 second in four individuals; these values are usually associated with a slow sinus rhythm.

The average value for the constant K of the formula used for electrical systole²⁶ is 0.388 ± 0.0022 (standard error). This value may be compared to that for normal Chinese males²⁸ as follows:

116 normal Chinese males	0.374 ± 0.0012
46 ricksha pullers	0.388 ± 0.0022
Difference	0.014 ± 0.004

There is a slight but probably not significant difference.

DISCUSSION

Although the number of ricksha pullers examined is relatively small, the data presented seem to warrant certain conclusions.

In the first place, about 50 per cent of the subjects had hearts that were demonstrably enlarged. This in itself, we believe, is an important and significant finding. Although previous careful studies of animals and of athletes have shown that cardiac hypertrophy is a natural result of prolonged muscular exercise, clinicians have usually held to the dictum that an enlarged heart is a diseased heart.²⁹ None of the individuals studied had any other sign of disease than cardiac enlargement (and in some cases widening of the aorta), and all were actively engaged in an occupation calculated to bring out such signs. It must be admitted that we have no post-mortem examinations to report, and, therefore, final proof is lacking. It is, however, a fair conclusion, as far as the evidence goes, that the cardiac enlargement found is probably related to the physical activity of the subjects.

The physiological basis for cardiac hypertrophy in response to prolonged unusual exercise is clear. Studies have shown that the minute volume put out by the heart may be raised to 20 or more liters in severe

exercise, and that in highly trained men the increase in minute volume output of the heart is obtained to a much greater extent by increase in the stroke volume of the heart and, to a much smaller extent, by acceleration of the rate. In the case of De la Mar, a Marathon runner, it was shown by Boek, Van Caulaert, Dill, and others³⁰ that his stroke volume at rest was double that of untrained subjects and during work it rose to 200 c.c. Similar results have been reported by Hill and Lupton.³¹

Bainbridge et al.³ point out the advantages of a powerful myocardium, with complete systolic emptying and but slight dilatation and tachycardia. He says, "Hence, for the making of an athlete, a large and muscular heart is just as much a physiological necessity as a highly developed muscular system, since, whatever the size of his muscles, a man's ability to perform muscular work is determined by the output of his heart."

The ricksha pullers examined must be considered to have been successful in their occupation, because they were not new at it and were selected by their employers from a large field of applicants. It must be noted here that the hypertrophy which we believe they showed may well not occur in all who endeavor to take up ricksha pulling.

Attention is called to the exact nature of the activity involved. It consists of running and pulling the ricksha, often for fair distances; but most important, this is done for a few hours a day, day after day for years, with few if any days of inactivity. There is no evidence to settle the point, but the suggestion may be made that running and other forms of extensive bodily motion may be more effective in producing cardiac changes than other forms of hard work. There can be no doubt that unintermitting daily activity for years would be more effective than intermittent or brief exercise. Even highly active athletes often have long intermissions in their periods of training.

In the second place, our results include evidence of widening of the aorta in some instances of relatively young men with no trace of syphilis. If this unusual finding in normal subjects has a physiological basis, the explanation can be found in the effect of the sustained increased blood pressure during exertion upon the elastic aortic wall.

Third, there arises the question whether such cardiac enlargement as was found is entirely physiological or not. In other words, is there such a disease as athletic heart?

As far as our results go, they give no indication for regarding the abnormal findings encountered as constituting or predisposing to disease. The men in whom cardiac enlargement was present had no evidence of the slightest heart failure and were holding their positions in competition with thousands of others. Many ricksha pullers continue in their occupation for long years, twenty and more years not being uncommon. One must also consider the men in our study who had been in their occupation for years without showing cardiac enlargement. They

also were successful. Possibly they should be regarded as being better adapted. Even this conclusion does not mean that the group with enlargement is, or will be, diseased, since it is merely a matter of relative fitness.

It is of course possible that, while the effects of prolonged exertion are purely physiological for the time being, they may accelerate the normal wear and tear of life. In that case they would not be direct but only contributory causes of death.

It is a common impression in China that the work of ricksha pullers is unduly hard, that damage is done to the heart and that the men cannot remain long in the occupation but die prematurely. The only reference in medical literature which we have found is in Chinese.³² This is a report of physical examinations of 36 ricksha pullers. The author found the apex impulse of the heart beyond the nipple line in every case, and considered this to mean cardiac enlargement. Bradycardia was common. The findings were attributed to the ricksha pulling and interpreted as constituting disease. Valvular lesions and rupture of cerebral vessels were considered possible consequences. No x-ray or other laboratory examination was made. Our impression is that ricksha pulling is not in itself unduly hard and could not be compared to the work of stevedores, for example. On the other hand the life of public ricksha pullers is extremely difficult because, owing to their very small earnings, they cannot feed, clothe, and house themselves properly, and because they are compelled to expose themselves for long hours to all the inclement weather which the climate imposes. It does not appear that they are engaged in pulling their rickshas for long periods, because of severe competition for passengers. If their lives are short, exposure and privation are probably responsible.

SUMMARY

1. Forty-six healthy Chinese ricksha pullers were examined in a study of the effect of chronic exertion on the cardiovascular system. Physical, roentgenological, and electrocardiographic studies were carried out.

2. The mean age was thirty-three years. The mean duration of ricksha pulling was eight years, and the mean number of hours of actual running slightly over three per day.

3. Twenty-one (45 per cent) of the 46 ricksha pullers showed definite cardiac enlargement on physical examination which was always performed before radiographic examination.

4. The measured frontal cardiac area of the teleroentgenogram of the heart was 15 per cent or more above the area calculated according to the method of Hodges and Eyster in 20 individuals (43 per cent).

5. The mean deviation of measured cardiac area of 140 normal Chinese males from the calculated area in per cent was minus 4.2 ± 0.68 (stan-

dard error). The mean deviation of measured cardiac area of the 46 ricksha pullers from the calculated area in per cent was plus 13.2 ± 2.3 . The difference between these two groups was 17.4 ± 2.38 .

6. The cardiothoracic ratio of Danzer in telecardiograms was 0.52 or greater in 22 ricksha pullers (48 per cent). The mean ratio of the telecardiograms of 116 normal Chinese males was 0.485 ± 0.004 .

7. Chronic exertion in the form of ricksha pulling caused cardiac enlargement in about 45 per cent of the subjects. No demonstrable enlargement was present in the remainder. This cardiac enlargement, probably chiefly due to hypertrophy, is considered to be a physiological response to rapid exertion carried on daily for a period of years. There is no indication that the enlargement constitutes or predisposes to disease.

Thanks are due to Dr. I. C. Yuan for his advice on the statistical treatment of the data in this paper.

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THE PATENCY OF THE SO-CALLED "ANATOMICALLY OPEN BUT FUNCTIONALLY CLOSED" FORAMEN OVALE*

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ZAHN¹ and Mönckeberg² indicate that under certain conditions the so-called "anatomically open but functionally closed" foramen ovale may become patent and lead to paradoxical embolism. Other reports in the literature add support to this contention, including the more recent publications of Beattie³ and of French,⁴ which give autopsy findings of emboli caught in the foramina ovale. It has been claimed that when the right auricular pressure exceeds the left auricular pressure, the functionally closed foramen becomes patent. Because this type of foramen ovale has not been universally recognized as a factor in the production of paradoxical embolism, the present study of the behavior of the foramen ovale under various differences in auricular pressures was undertaken.

METHOD

The interauricular septum of hearts with open, valvelike foramina ovale, removed at autopsy, is clamped by means of four screws between two flanged metal plates that have a circular opening completely exposing both sides of the foramen ovale. (Fig. 1.) Two glass cups (C) with three side openings are cemented to the flanges and function as artificial atria. Instead of blood, a fluid is used which consists of 0.32 per cent tragacanth suspended in 0.9 per cent saline. The viscosity and the osmotic pressure of this suspension are approximately that of blood. The height of the reservoirs (R) holding this fluid determines the auricular pressure which is measured by a straight manometer tube (M) connected with the artificial atrium by means of the middle side tube. The second side tube connects with the reservoir. The third side tube is clamped off and serves as a vent for the escape of air caught in the apparatus. Artificial emboli are prepared by mixing "Yatex"† (a concentrated form of Latex) with plaster of Paris in a proportion so that the small pieces (1 × 1 × 2 mm. to 2 × 2 × 3 mm.) just about sink in the fluid. The mixture consists of 3.2 gm. Yatex and 1 gm. plaster of Paris. These pieces, ten to twenty in number, are introduced into the right atrium. Before each experiment the apparatus is tested for leakage, under a pressure of 400 mm. of fluid.

During the course of the experiment the height of the right reservoir is increased on several occasions so that various degrees of predominance in right auricular pressure are obtained. Due to the higher level of fluid in the right reservoir, a flow of the fluid is established through the foramen ovale from the right into the left reservoir. The heights of the fluid level in the reservoirs are recorded at the start and after one minute of flow. The auricular pressures as shown by the manometer in millimeters of fluid are also recorded at the start of the

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flow and during the flow. The change in volume in either reservoir during this time indicates the flow in one minute through the foramen ovale. Similar observations are made when the level of the left reservoir is raised higher than that of the right so that there is a predominance of pressure in the left atrium. During a period of flow under a maximum predominance of right auricular pressure the apparatus is shaken with both hands to agitate the artificial emboli in the right auricle. At the end of one minute of such flow, the emboli in the left auricle as well as the emboli caught in the foramen are counted.

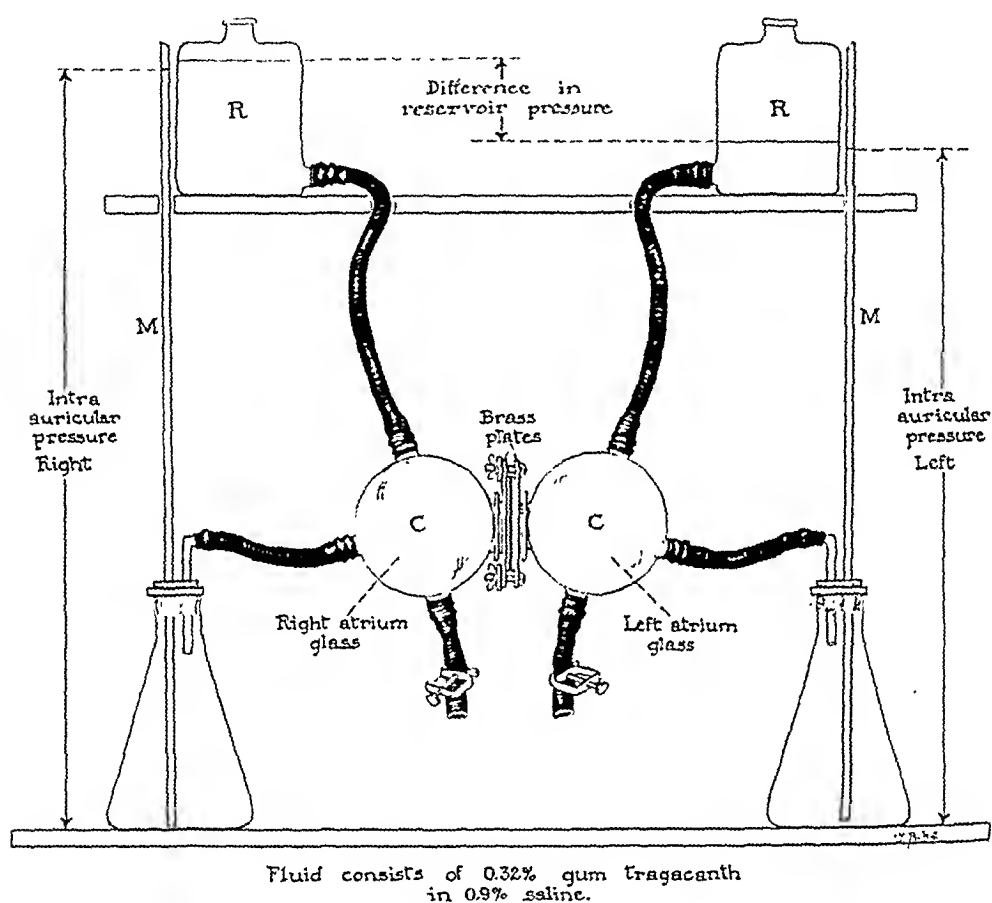


Fig. 1.—Diagram of apparatus.

RESULTS

With the fluid level of the right reservoir higher than that of the left reservoir and the tubing connecting with the left reservoir pinched off, the left auricular pressure may be equal to the right auricular pressure or may even exceed it. This paradoxical condition is explained by the fact that the foramen ovale behaves as a valve and transmits pressure freely in one direction only. As soon as the tubing to the left reservoir is opened, a drop in both auricular pressures occurs. This drop is greater on the left side. As the flow is maintained, the left auricular pressure begins to rise slowly while the right auricular pressure falls slowly. However, during the minute of flow, the right auricular pres-

sure is always greater than that of the left. When, at the end of one minute, the tubing to the left reservoir is again pinched off, both auricular pressures rise to a level commensurate with the fluid level in the right reservoir; and again the left auricular pressure may rise to a slightly higher level than the right because of the valvelike action in the foramen ovale. The fluid level of the right reservoir descends, while that of the left reservoir rises correspondingly from the time that the tubing to the left reservoir is opened to the moment that it is pinched

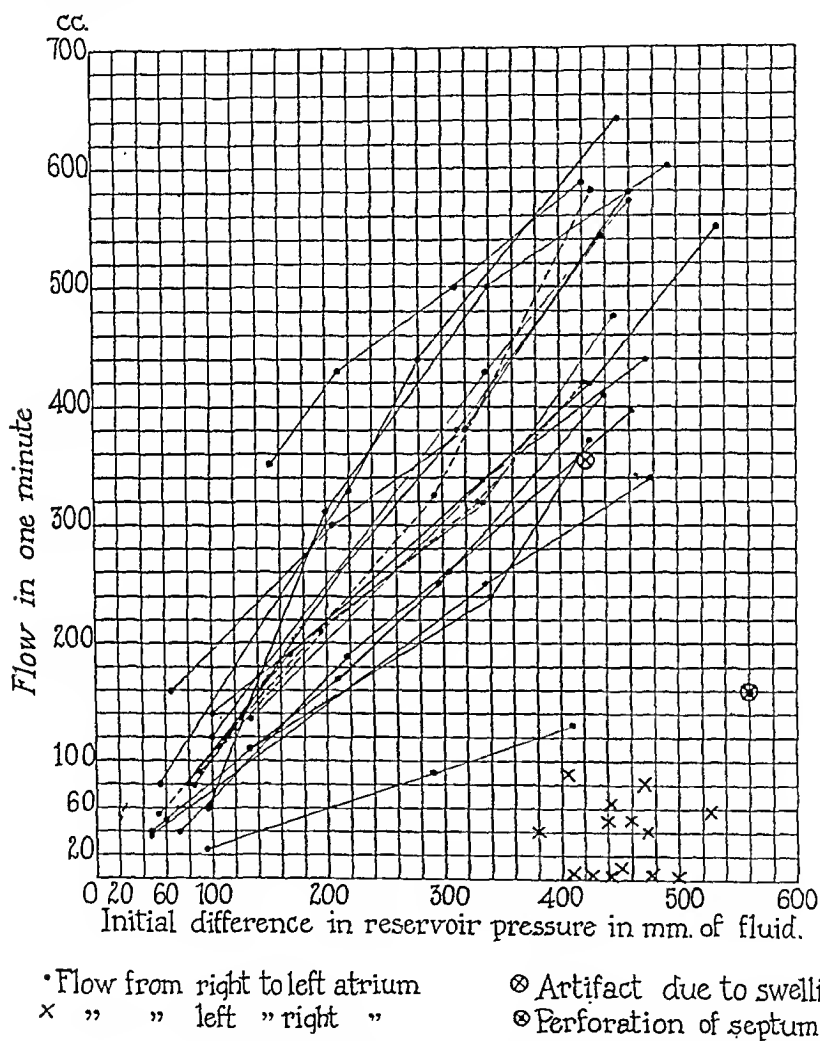


Fig. 2.—Graph showing relationship between the difference in reservoir pressure and the flow through the foramen ovale.

off again. The volume of flow from right to left increases with the degree of preponderance of right auricular pressure. The results of experiments performed on sixteen patent foramina ovale are listed in Table I. The graphical representation of the relationship between the leakage through the foramen ovale and the difference in reservoir pressure is shown in Fig. 2. It is seen that an almost linear relationship is indicated.

TABLE I—CONT'D

NO.	CIRCUMFERENCE OF FORAMEN	INITIAL PREDOMINANCE IN RIGHT RESERVOIR PRESSURE mm.	TERMINAL PREDOMINANCE IN RIGHT RESERVOIR PRESSURE mm.	INITIAL AURICULAR PRESSURES		AURICULAR PRESSURES DURING FLOW		TERMINAL AURICULAR PRESSURES		FLOW IN ONE MINUTE c.c.
				RIGHT	LEFT	RIGHT	LEFT	RIGHT	LEFT	
9	22	413 332 168	304 245 128	589 588 360	589 590 360	448 474 300	376 417 272	542 548 340	542 548 340	420 320 190
10	28	87 439 294 210	67 352 235 157	586 558 556 327	590 558 556 327	555 385 438 240	546 352 418 228	578 514 524 304	582 514 524 304	90 410 250 170
11	40	60 460 320 205	48 228 238 127	560 528 278 482	560 528 278 482	540 432 454 525	530 365 426 487	556 507 244 425	556 507 244 425	50 580 380 300
12	12	65 425 340 133	40 332 278 92	568 145 226 496	568 145 226 494	555 450 482 578	545 124 274 507	508 187 252	508 187 252	160 370 240 105
13	8	47 410 290	42 366 273	450 572 558	446 563 552	557 554 492	498 212 274	525 556 523	510 548 510	40 130 90
14	28	96 429 293	87 347 196	580 656 560	568 648 670	576 366 416	512 313 388	586	568	25 590 325
15	23	54 479 387	40 386 271	559 606 608	568 577 577	535 454 497	533 247 338			55 340 250
16	23	43 474 338	34 360 248	543 605 590	530 604 606	535 400 453	490 285 378			39 440 335
		131	92	606	625	551	543			135

Occasionally emboli pass spontaneously through the foramen ovale, but generally emboli pass through the foramen ovale or are caught in it only after the apparatus has been shaken vigorously and the emboli thereby set into motion. Table II shows the relationship between the circumference of the foramen, the preponderance of the right auricular pressure, the preponderance of the right reservoir pressure, and the number of emboli which passed through, or were caught in the foramen ovale. No determination of the transmission of emboli was made on heart numbers 1 and 3. The only foramen ovale of those investigated which did not allow emboli to pass into or through it was number 13. The probable explanation for the behavior of this foramen is to be found in its small size.

TABLE II

NO.	CIRCUM- FERENCE OF FORAMEN	PREDOM- INANCE OF RIGHT RESERVOIR PRESSURE	PREDOM- INANCE OF RIGHT AURICULAR PRESSURE	NUMBER OF EMBOLI CAUGHT IN FORAMEN	NUMBER OF EMBOLI WHICH PASSED THROUGH THE FORAMEN
2	32	680	230	0	9
4	25	437	—	0	2
5	40	281	10	0	1
5	40	221	15	0	2
5	40	452	15	0	3
6	25	456	103	1	0
7	16	447	—	5	0
8	24	474	—	3	2
9	22	332	60	0	1
9	22	413	72	1	2
10	28	439	33	3	2
11	40	460	67	2	3
12	12	425	326	1	0
13	8	410	342	0	0
14	28	429	53	0	5
15	23	479	159	0	4
16	23	510	—	7	4

When the predominance of pressure is shifted to the left side and the tube communicating with the right reservoir is pinched off, the right auricular pressure may correspond to the right reservoir pressure, or it may be higher. When the tubing to the right reservoir is opened, the right auricular pressure drops according to the fluid level of the right reservoir. In a few foramina ovale no subsequent increase in right auricular pressure occurs; nor is there a change in fluid level in either reservoir. In other words, some patent foramina ovale allow no leakage of pressure or fluid from left to right. In the larger number of cases, on releasing the pinched-off tubing, there is an immediate rapid drop of right auricular pressure to a level commensurate with the right reservoir fluid level. This is followed by a slight gradual rise in right auricular pressure accompanied by a slight drop in the fluid level of the left

reservoir and a coincidental rise in fluid level of the right reservoir. The greater the predominance of left auricular pressure, the greater the amount of leakage through the foramen ovale. With the exception of two instances, the amount of flow through the foramen ovale from left to right is slight compared with the flow from right to left at similar differences in pressure. The two discrepancies where considerable leak-

TABLE III

NO.	CIRCUM- FERENCE OF FORAMEN	PREDOM- INANCE OF LEFT RESERVOIR PRESSURE	AURICULAR PRESSURE DURING FLOW		FLOW IN ONE MINUTE
			RIGHT	LEFT	
1	30	445	No change		0
2	32	500	No change		0
3	Three small openings 1-2 mm.	474	115	569	40
4		423	290	468	355
5		561	83	550	162
6	25	470	156	582	83
7	16	529	173	571	58
8	24	450	46	592	10
9	22	406	278	486	90
10	28	380	—	—	40
11	40	460	—	—	50
12	12	425	No change		0
13	8	410	No change		0
14	28	442	163	506	66
15	23	476	133	603	0
16	23	440	155	555	50

age occurred from left to right are explained in one by a perforation in the septum, and in the other by a severe distortion of the foramen from edema secondary to clamping. The results of these investigations are tabulated in Table III and indicated in Fig. 2.

COMMENT

The results obtained indicate that the so-called anatomically patent, functionally closed foramen ovale transmits pressure, fluid, and suspended solids from the right to the left atrium when the right auricular pressure exceeds that of the left. These findings are in accord with the observations and conclusions of Zahn,¹ Mönckeberg,² Beattie,³ French,⁴ Chiari,⁵ and others.

Zahn collected 139 cases which at autopsy had a patent foramen ovale. Among these cases, he found two with thrombotic occlusion of the foramen and seven with paradoxical embolism. In addition, he listed a third case, referred to him, of thrombotic occlusion of the foramen ovale. Zahn believed the explanation of paradoxical embolism to lie in the fact

that in congestive heart failure there is an elevation in right auricular pressure with a coincidental reduction in left auricular pressure. In all nine cases, evidence of venous stasis conditioned by chronic bronchitis, pulmonary emphysema, edema, atelectasis, tuberculosis or pleuritis was found. The anatomical evidence pointing to a previously existing congestion and elevation of pressure in the right heart consisted of dilatation and hypertrophy of the right auricle and ventricle, the enlargement of the fossa ovalis and the bulging of its wall to the left.

Beattie reported a case of pulmonary embolism which, at autopsy, showed occlusion of the pulmonary artery by an embolus and a second embolus caught in the foramen ovale. This foramen ovale was of the type considered anatomically open but functionally closed. Beattie inferred that the embolic occlusion of the pulmonary artery preceded the embolic occlusion of the foramen ovale. He contended that the embolic occlusion of the pulmonary artery caused an elevation of the right auricular pressure and a coincidental fall in the left auricular pressure which forced the foramen ovale open and allowed the second embolus to slip in and lodge there. He indicated that in all probability the reason for the patient's survival for a short time after the pulmonary occlusion was the patent foramen ovale which allowed the blood to be shunted across to the left atrium. He suggested that patency of the foramen ovale be kept in mind to explain similar short survivals following pulmonary occlusion.

The apparatus used in these investigations does not reproduce the rapid movement of fluid with eddies which are present in the living heart. It is therefore necessary to agitate by shaking, but this also appears inadequate. It is possible that with a modification of the apparatus to provide for a brisk flow of the fluid with a production of eddies, a larger number of emboli would pass through the foramen ovale under the same pressure conditions.

A valvelike action of the foramen ovale is established by its capacity, in some cases, to prevent completely the leakage of pressure and fluid from left to right, and in other instances to transmit comparatively very little fluid to the right atrium. This valvelike action is due to the tenuity and pliancy of the septum primum and the relative thickness and rigidity of the septum secundum.

There are no data available on human left and right auricular pressures, and the pressures used in these experiments may very well be beyond the pathological limits occurring in man. Nevertheless, the behavior of this type of foramen ovale under these experimental conditions is probably a good indication of the behavior clinically under certain pathological conditions.

CONCLUSIONS

These investigations on the so-called anatomically open but functionally closed foramen ovale furnish experimental proof for the following statements:

1. Under conditions of preponderance of pressure in the right atrium over the left, pressure, fluid, and emboli may be transmitted from the right atrium through the foramen ovale into the left atrium.
2. When the left auricular pressure is greater than the right, comparatively little or no transmission of pressure or fluid from the left atrium to the right atrium occurs due to a valvelike action of the foramen ovale.

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THE ELECTROCARDIOGRAM OF THE NORMAL HEART IN PREGNANCY*

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IF THE electrocardiogram is to aid us in the interpretation of the signs and symptoms referable to the cardiovascular system in pregnant women, we must be acquainted with the influence that pregnancy, due to a rising uterus, may have on it.

That the electrocardiogram undergoes certain changes when the position of the heart within the chest is altered, has been long appreciated. Einthoven showed that deep breathing affected the form of the electrocardiogram, as it changed the position of the heart, the more transverse position at the end of expiration being associated with a left axis shift, or a tendency in that direction. Cohn demonstrated that there is a rather definite relation between the anatomical angle of the heart (angle of inclination) and the direction of the electrical axis. Thus the electrocardiogram shows a gradually increasing left axis deviation as the position of the heart becomes more transverse, and right axis deviation as the heart becomes more vertical.

But that pregnancy may change the electrical axis of the heart by a rising diaphragm is not widely known. Smith showed that during the eighth month of pregnancy when the uterus is at the highest level in the abdomen, the electrocardiogram displayed a left axis deviation. This became less marked as soon as the head of the fetus descended into the pelvis, and shifted toward the right immediately after the delivery of the child. Konki studied 33 pregnant women with normal hearts, and he found that during the third trimester of pregnancy, the electrical axis deviated to the left, and that the T-wave in Lead III became negative. Following the delivery the axis shifted to the right, and the T-wave in Lead III became upright. He quotes Hynemann, who affirms that the diaphragm of pregnant women during the early part of the third trimester is elevated on the right side on the average of 2.10 cm. and on the left side by 2 cm. and that the heart has assumed a more transverse position. Jensen and Norgaard reported that in their series of pregnant women there was a left axis deviation or a tendency thereto during the first months of pregnancy and a return to the right in the later months. They say that this is due to an early left ventricular hypertrophy, followed later by a right ventricular hy-

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peritrophy, independent of any change in the position of the heart. These observations led us to study the electrocardiogram in pregnancy.

After we began our investigation, an article appeared by Carr and Palmer, who found that the axis tends to shift to the left during the first two trimesters of pregnancy and to the right in the early part of the ninth month. The latter finding they attribute to the descent of the uterus.

Material.—Thirty-six pregnant women were selected. These patients had no complaints referable to their cardiovascular system, and upon examination their hearts and vascular systems were found to be normal. In selecting these patients, age and the number of the pregnancy were not considered. These women were sent down to the electrocardiographic laboratory some time between the thirty-second and thirty-sixth weeks of pregnancy, when the uterus was considered to be at the highest level in the abdomen. This procedure was strictly supervised by one of us (H.H.H.). The second electrocardiogram was taken about eight or ten days after delivery when the patient was ready to go home. At first we took a third electrocardiogram, six weeks post partum. But the latter was soon abandoned, since we found no difference between it and the second electrocardiogram. The electrocardiograms were taken with the patient in the sitting position. The electrical axis was calculated, according to Einthoven, from the electrocardiogram.

RESULTS

Direction of the Electrical Axis.—The influence of pregnancy on direction of this axis is shown in Table I. Only those tracings showing a shift of more than 10 degrees in the electrical angle were recorded. Twenty-one of the 36 cases studied (58.33 per cent) showed such changes.

It will be seen that there is usually definite shifting of the electrical axis toward the left during this period of pregnancy, and to the right in the puerperium. The first case has an angle of -2 degrees which is slight axis deviation (considering $0-90$ as normal). Following the delivery the angle changed to 49 , which is normal. The next two cases with an electrical axis of " 0 " may be considered as having a tendency to left axis deviation. Their axis, too, became normal following the delivery. Cases 4, 5, 6 and 7 may be considered as having only a slight tendency toward left axis deviation, which became normal after the delivery. The next six cases are, as considered by some,⁷ at the lower limits of normal. The greatest shifting of the axis toward the left was noticed in Case 9. Before delivery the angle was 10 degrees and after delivery 90 degrees; in other words from the lower to the very upper limits of normal. Cases 14, 15, 16 and 17 had each an angle of 30 degrees before delivery. During the first week of puerperium this angle changed to 72° , 58° , 55° , and 60° respectively. Cases 18, 19, 20

and 21 had angles which are considered just normal, and the shift to the right following delivery was not very marked, the largest being 20° and the smallest 13° . Thus, in the entire series the shift to the right in puerperium varied from one of 13° to one of 80° . The average direction of the electrical axis between the thirty-second and thirty-sixth weeks of pregnancy in this series was 19° , and a week after the delivery 57° . The average difference, thus, in the axis was 38° in a counter-clockwise direction, or shifting to the left. This figure is greater than that reported by Carr and Palmer, whose difference is only 27° to the left in four cases in which an electrocardiogram was taken after delivery.

TABLE I

INFLUENCE OF PREGNANCY ON DIRECTION OF THE ELECTRICAL AXIS AND ON T_2 -WAVE IN THE NORMAL HEART

PREGNANCY 32-36TH WEEK			PUERPERIUM FIRST WEEK		DIFFERENCE IN THE ANGLE
CASES	ANGLE	T_2^*	ANGLE	T_2^*	ANGLE
1	-2°	-	49°	-	51°
2	0	\pm	58°	+	58°
3	0	-	43°	\pm	43°
4	3°	-	52°	+	49°
5	3°	-	52°	-	49°
6	3°	-	52°	-	49°
7	4°	-	30°	-	26°
8	10°	-	50°	+	40°
9	10°	-	90°	\pm	80°
10	12°	-	52°	\pm	42°
11	15°	-	55°	-	40°
12	17°	-	50°	-	33°
13	18°	+	65°	+	48°
14	30°	-	72°	-	42°
15	30°	-	58°	-	28°
16	30°	-	55°	-	25°
17	30°	-	60°	-	30°
18	40°	0	58°	+	18°
19	42°	-	62°	-	20°
20	51°	-	64°	+	13°
21	53°	+	70°	+	17°
Averages	19°		57°		38°

*+means upright.

- means inverted.

\pm means diphasic.

0 means flat or isoelectric.

Our results correspond with those of the authors mentioned, although our procedure was somewhat different. Taking into consideration what is known about the influence of the position of the heart on the electrocardiogram, it is logical that, at a certain stage of pregnancy, when the diaphragm is very often pushed up so that the heart lies in a comparatively transverse position, there should be a shift of the electrical axis to the left. (Fig. 1.) The type of the individual also plays a great part; the hypersthenic patient during pregnancy will show more deviation to the left than will the opposite type. This factor, besides the size of the baby and the amount of amniotic fluid, may be responsible for the

difference in the degree of the shift in different patients, or for the absence of an appreciable deviation in others. That is, a fairly high diaphragm with a small uterus may produce more shifting than a low diaphragm with a good-sized baby.

Recent studies in obesity^{8, 9} show that the position of the diaphragm is often responsible for left axis deviation and changes in Lead III. The electrocardiogram returned to normal in the great majority of patients

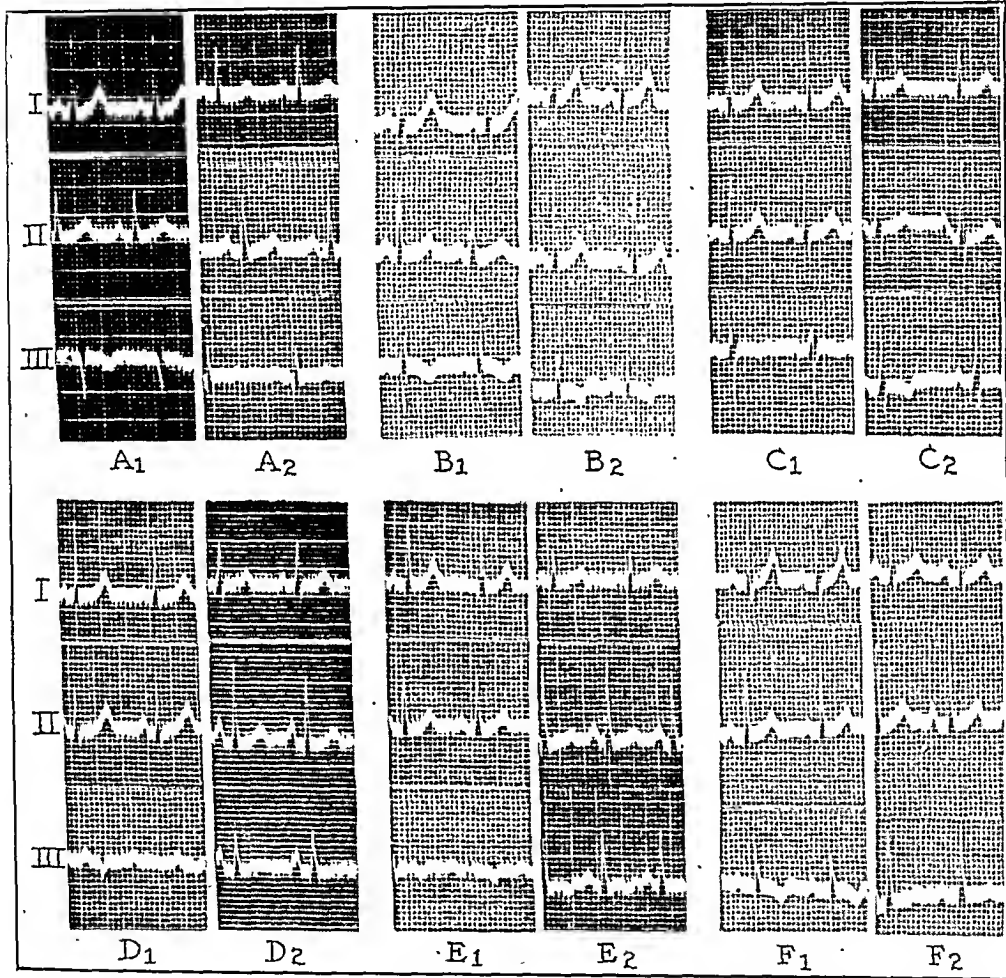


Fig. 1.—Six pairs of electrocardiograms to show the variations which may be encountered in Lead III during pregnancy. In each case, the first electrocardiogram was taken between the thirty-second and thirty-sixth weeks of pregnancy and the second during the first week of the puerperium.

who lost weight by dieting. Kimura studied the roentgenograms and the electrocardiograms of patients with big ovarian tumors. The heart occupied a more or less transverse position in the chest, and the electrocardiogram showed a tendency to left axis deviation. The T-wave in Lead III became flattened or inverted. After removal of the tumor the heart became more vertical, and the electrocardiogram shifted toward the right, and the T-wave in Lead III assumed an upright position

Bland and White in studying one hundred electrocardiograms with complete inversion of Lead III showed that 72 per cent of the patients had a high diaphragm and a transverse position of the heart, and that 55 of these were obese individuals. All these studies tend to show that it is the position of the heart and not the questionable transient hypertrophy that is responsible for the shifting of the axis toward the left.

Changes in the P-wave in Lead III.—We have encountered two records with an inverted P_3 . One was associated with an inversion of the entire Lead III, besides an inverted P_2 , and the other occurred in an otherwise normal electrocardiogram. Both remained unchanged during the puerperium, in spite of the fact that the other complexes of the inverted lead, as well as the inverted P_2 , became upright. There was a definite tendency, however, for the P-wave in Lead III to become more defined and of a somewhat higher voltage after the delivery. However, it seems that the influence of pregnancy on the P-waves is only slight and of little significance.

Changes in the Q-wave in Lead III.—Five records with large Q-waves in Lead III, according to the criteria of Pardee, were found in this series of 36 cases. They were all associated with inverted T_3 . Three of these large Q-waves in Lead III disappeared after pregnancy (see B_1 and B_2 , Fig. 1). In one of these the negative T-wave in Lead III became flattened, and the R_3 became somewhat higher. In the remainder the T_3 was not changed. According to the recent literature,^{13, 14} the large Q-wave in Lead III during pregnancy is taken to signify a transverse position of the heart due to elevation of the diaphragm. That the deviation of the septum from its usual position, as well as the transverse position of the heart, may be a factor in the production of Q_3 , has been suggested.¹⁴ The incidence of the large Q_3 in our series is about the same as that reported by others. It is of interest that the incidence of the larger Q_3 in normal hearts in pregnancy is very much greater than in normal hearts in a control series.^{12, 13} Evidently the altered position of the heart is a large factor in this change.

Changes in T-wave in Lead III.—Of the 21 cases that showed marked changes in direction of the electrical axis, T_3 was completely inverted in 17; in one it was flat, in one diphasic and in two upright. During the puerperium the T_3 was negative in 11 cases, diphasic in 2, and upright in 8; in other words a gain of one diphasic T_3 and 6 upright ones. (See Table I.) Left axis deviation or tendency thereto, due to a change in position of the heart, is usually associated with an inverted T_3 .^{2, 11} Our records bring this out. Table I shows that the first upright T in Lead III is seen in Case 13, whose angle is 18° . The next one is seen in the last case, whose angle is 53° . During the puerperium the appearance of the upright T-wave in Lead III was usually associated with angles

of 50° or over, which is considered normal. On the other hand, in no instance did a positive T_3 during pregnancy become changed after the delivery.

There were four records which showed no changes in the electrical axis but had negative T_3 . After the delivery, one such became diphasic, one flat and two upright. Hence by adding these two groups showing changes in T_3 we find that out of 25 records, an inverted T_3 was seen in 21 patients before delivery and only in 11 after—a change of 47.61 per cent toward the upright.

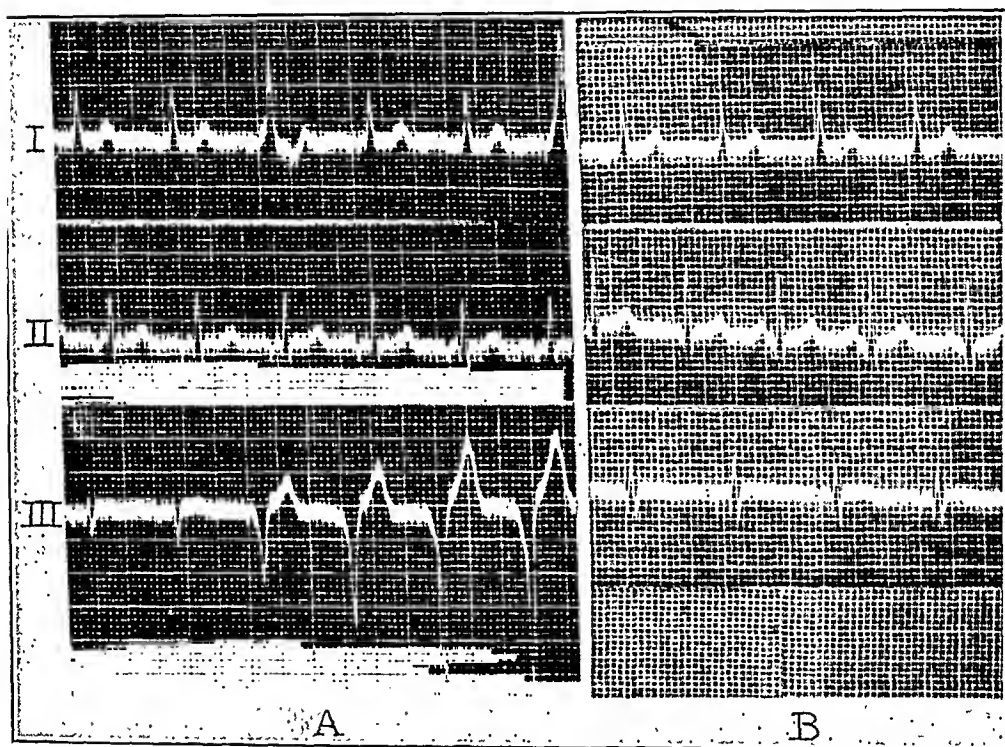


Fig. 2.—A, Two electrocardiograms of the same patient. A was taken between the thirty-second and thirty-sixth weeks of pregnancy. Rate is 105. Frequent extrasystoles in Lead I, and P_2 and P_3 are inverted. Lead III shows a run of ventricular tachycardia.

B was taken during the first week of puerperium. Rate is 96. Arrhythmia disappeared. P_2 has become positive. Note the change of the direction of the electrical axis.

Pardee states that a downward T_3 may be due at times to a high position of the diaphragm. This would tip the apex of the heart upward and would tend to produce a relatively small or even inverted T_3 , just as it tends to produce a small or inverted R_3 . The variations in the direction of the electrical axis within the heart, giving rise to the T-wave are modified by the position of the heart in the body. The changes in the T-waves in Lead III in our series can probably be accounted for by the high position of the diaphragm. Thus the heart has moved, as we view the patient from the front, in a counter-clockwise direction when

the uterus has reached its highest level in the abdomen, and in a clockwise direction as soon as the uterus has emptied itself.

Arrhythmia.—One of our records showed frequent ventricular extrasystoles terminating in a short paroxysm of ventricular tachycardia. This was observed on several occasions between the thirty-second and thirty-sixth weeks of pregnancy. The rate per minute was over 100 each time, and the patient was very uncomfortable. She was conscious of these "skipped beats," and she experienced some dyspnea. In the electrocardiogram taken after the delivery, the arrhythmia was absent, and the pulse rate was lowered somewhat (Fig. 2). The symptoms also disappeared. Premature contractions have been known to exist during pregnancy and labor. According to Maekenzie, this arrhythmia occurs very frequently during pregnancy. It is of interest to note that the comparatively rapid heart in our patient did not prevent the appearance of these premature contractions. It is possible that some product of the metabolism in pregnancy is responsible for the production of this arrhythmia.

SUMMARY

1. The electrocardiograms of 36 pregnant women with normal hearts were studied. One electrocardiogram was taken some time between the thirty-second and thirty-sixth weeks of pregnancy, and a second during the first week of puerperium.

2. Twenty-one cases (58.33 per cent) showed a left axis deviation or tendency thereto during the time when the uterus was at its highest level in the abdomen. The smallest deviation in a counter-clockwise direction was 13° and the largest was 80° , the average being 38° . The axis shifted to the right following delivery.

3. An inverted T_3 was seen in 17 of the 21 records showing axis deviation. Two were positive, one was isoelectric, and one was diphasic. During the puerperium there appeared only 11 inverted, 8 positive, and 2 diphasic T_3 . Four records, not showing any change in the axis, showed T_3 inverted during pregnancy, and after delivery in two instances this became upright, in one isoelectric and in one diphasic (11.11 per cent).

4. Three records of the 36 (8.33 per cent) showed a large Q_3 which disappeared following the delivery.

5. One case (2.61 per cent) had frequent ventricular extrasystoles, terminating in a short run of ventricular tachycardia. After the delivery this arrhythmia disappeared.

6. Adding the changes seen in the axis, T-waves alone, the large Q_3 , and one case of arrhythmia, we have an incidence of 80.88 per cent in our series that showed changes in the electrocardiogram during a time when the uterus was at its highest level in the abdomen. (Table II.)

7. These findings corroborate those found in the literature and are compatible with the interpretation that during this stage of pregnancy

the heart assumes a comparatively transverse position due to the elevation of the diaphragm.

TABLE II

THE INCIDENCE OF CHANGES IN THE ELECTROCARDIOGRAM OF THE NORMAL HEART
IN THIRTY-SIX PREGNANT WOMEN

CHANGES	CASES	PER CENT
Changes in angle and T ₂	21	58.83
Large Q in Lead III	3	8.33
Changes in T ₂ alone	4	11.11
Changes in rhythm	1	2.61
Total	29	80.88%

8. When interpreting an electrocardiogram of a pregnant woman, one should bear in mind that at a certain stage of pregnancy left axis deviation, or tendency thereto, may often be found; that a large Q₃ may frequently be seen; and that extrasystoles are not rare. These findings disappear as soon as the uterus empties itself.

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Department of Clinical Reports

ELECTROCARDIOGRAMS FROM A FOUR AND A HALF MONTHS OLD FETUS

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THE diagnosis of incarcerated retroversion of a four months' pregnant uterus with threatened abortion was made on a twenty-seven-year-old colored woman, and laparotomy was decided upon. Dr. Martha Elizabeth Howe and I made preparations to take electrocardiographic tracings of the fetus, hoping at first that this could be done with the fetus in the uterus, before the removal of the uterus from the abdomen. However, at operation the findings were as follows:

The rectosigmoid junction and a fresh left pus tube were densely adherent to the anterior surface of the uterus, 1 cm. above the vesical fold of the peritoneum. In separating the adhesions the uterine wall had to be sacrificed to save the intestine, and a ragged tear was thus made with free bleeding and protrusion of the placenta. A supravaginal hysterectomy and bilateral salpingectomy were performed without, of course, opening the uterus in the abdomen.*

Immediately after removal, the uterus was opened, and the fetus, measuring 21 cm. in length, was removed, the connection between fetus and placenta being allowed to remain intact. The heart could be seen to be beating vigorously and continued to contract for approximately forty-five minutes. During this period we obtained the accompanying tracings.

Ordinary copper wire was used for electrodes, one end of the wire being inserted under the skin and the other end attached to the lead cables of a Sanborn portable electrocardiograph. The first three electrocardiograms were obtained with one electrode at the apex of the heart and the other just below the angle of the left scapula. An effort was made to obtain limb leads also, but only Lead II could be successfully recorded.

Tracing *A* was taken with the fetus attached to the placenta; that is, with the umbilical cord intact. *B* was taken with the cord firmly clamped. The general contour of the complexes is very similar to those

*The gynecological data were supplied by the operator, Dr. F. S. Fetterman.

of *A*, but the T-wave is less deeply inverted. *C* was taken several minutes later when the rate was beginning to slow. *D* was taken with the electrodes inserted under the skin of the right wrist and left ankle.

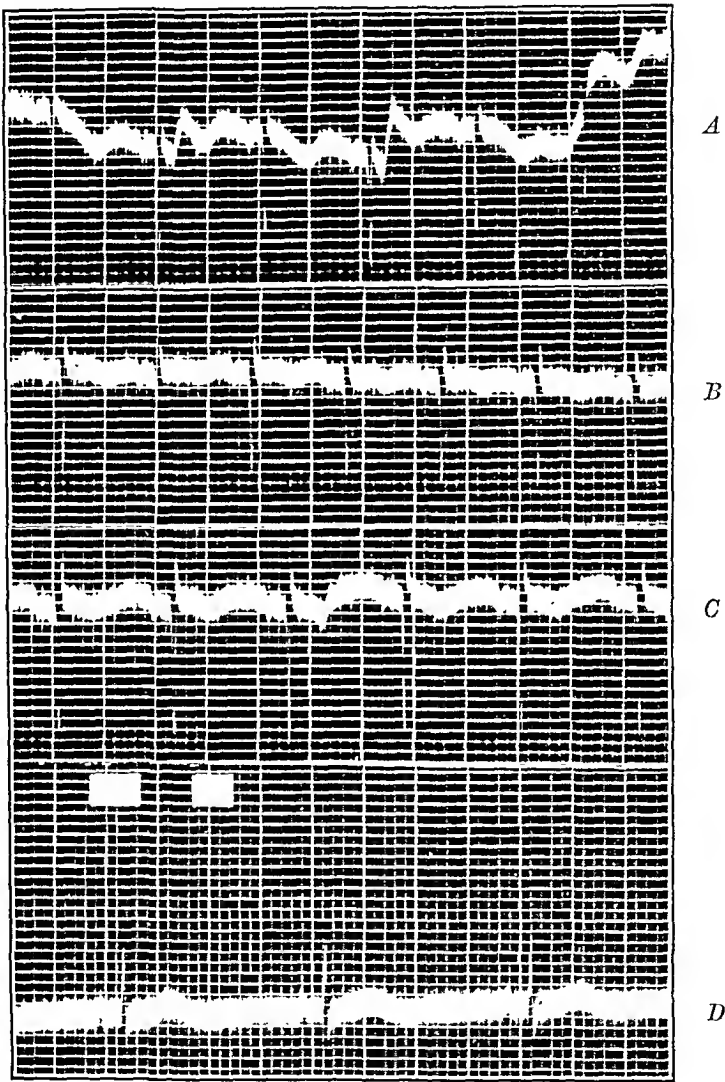


Fig. 1.—Electrocardiograms from a four and one-half months' fetus. *A*, *B* and *C*. chest leads—*A*, fetus attached to placenta; *B*, umbilical cord clamped; *C*, same as *B*, several minutes later, rate slowing. *D*, limb lead (right arm, left leg).

In general contour and direction of complexes it resembles the adult type of electrocardiogram.

As far as I have been able to ascertain, no electrocardiographic records from so young a fetus have been published prior to this time.

FREE BALL THROMBUS OF THE LEFT AURICLE*

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THE presence of a free ball thrombus in the heart is so rare as to be classed almost as a clinical and pathological curiosity. According to Covey, Crook, and Rogers,¹ twenty-three cases had been reported up to the appearance of their paper in 1928. These, together with their case, plus those of Schwartz and Biloon² and ours, make a total of twenty-seven, of which thirteen were diagnosed or suspected during life. According to the criteria of Hewitt,³ the two chief requirements for this diagnosis are that (1) it must be larger than the orifice in front of it, and (2) it must have a smooth surface and show no signs of former attachment. A number of thrombi have been wrongly considered as free when in reality they have been accidentally torn loose from their attachment by the manipulations of the pathologist in opening the heart. Practically, it is a matter merely of academic interest to distinguish, if it were possible, between a free thrombus and a pedunculated one, since both can act in the same way in producing symptoms.

It is our purpose to present an additional case and to discuss a few of the salient points in the clinical picture and the diagnosis.

REPORT OF CASE

A. K., female, fifty-three years old, was admitted to the Jewish Hospital on March 26, 1932, complaining of generalized aches, pains, and fever. Four days previously she had had dizzy spells and had become white and cold. There had been nausea and vomiting as well as some fever and cough for two days. She dated her first symptoms eight years before this entry when she began to have precordial pain and palpitation. Five years after the onset of her first symptoms she had been admitted to the hospital with the heart severely decompensated. At that time the diagnosis of auricular fibrillation, chronic myocarditis, and chronic passive congestion of the liver and lungs was made. With rest in bed and digitalization she quickly improved and was discharged from the hospital.

On her present admission she was deeply cyanotic and dyspneic, the heart was enlarged, and a systolic murmur was heard over the whole precordium, rougher over the aortic area than elsewhere and transmitted to the neck vessels. Mitral stenosis as indicated by a presystolic apical murmur and auricular fibrillation were present, the apex and radial rates being 84 per minute. Over the lungs, which were emphysematous, coarse rhonchi were heard which later disappeared. The abdomen was tympanitic, and the liver was felt two fingerbreadths below the costal margin. The reflexes were normal, no pathological toe signs being elicited. She was given relatively small doses of tincture of digitalis (1 c.c. daily) and became comfortable and symptom-free for the next ten days when she was allowed to be up and about.

*From the medical service of Dr. L. Sale, Jewish Hospital of St. Louis.

On April 7, 1932, she began to complain of sudden pain in both lower extremities and of marked coldness of the legs and cried out that she was dying. The arms and hands were found to be cold, while the finger tips were slightly cyanotic. In addition, too, the legs were cold, pale, cyanotic, and there was tenderness over the tibial ridge. The dorsalis pedis, popliteal, and femoral pulsations could not be felt. The pupils were dilated and reacted to light and accommodation. The heart was generally enlarged; the apex and radial rates were 72. On auscultation the precordial murmur was unchanged, and the second sound was accentuated everywhere. The blood pressure was 230/80 mm. It was thought that she had developed an embolus just above the bifurcation of the aorta. The next day both lower extremities were cold and pale from just below Poupart's ligament downward, the right leg being a trifle mottled. There was well-marked hyperesthesia from the middle of the thighs to the knees, while from the knees downward there was anesthesia. The femoral, popliteal, and posterior tibial pulsations remained impalpable. On the third day there was no indication of gangrene, the color of the legs had improved, and except for the toes the extremities had become warm, an improvement which had become definite within forty hours of the onset of symptoms.

On April 17, 1932, she suddenly began to gasp for breath and complain of chest pain. She was found sitting up, breathing hurriedly and heavily, apparently in agony. The chest pain was localized to the lower precordium. Her complexion was as usual, and examination of the heart revealed no new findings. The right radial pulse was markedly weaker than the left; the blood pressure could not be obtained on the right arm, while on the left it was 220/90. This attack quickly subsided, and it was at this time that the presence of an occluding ball thrombus of the left auricle was suspected for reasons which will be discussed later. The next day the right radial and brachial pulsations were still very feeble, but the arm was warm and seemed to be somewhat spastic.

She steadily lost ground, getting weaker and the extremities becoming quite cold again. The pulse could hardly be palpated anywhere, and she lapsed into coma, dying April 25, 1932, eighteen days after the onset of symptoms of peripheral circulatory disturbance and thirty days after her admission.

Autopsy Findings.—The pertinent findings at the post-mortem examination which was done by Dr. Sam Gray were as follows:

Heart: The heart was somewhat enlarged, the hypertrophy occurring chiefly in the right ventricle. The musculature of the left auricle was also hypertrophied. The tricuspid, pulmonary and aortic valves were thin and delicate and presented no deviation from the normal. The mitral valve was very thick and hardened, and the leaflets were fused, presenting at its opening a mere slit measuring $4 \times \frac{1}{2}$ cm. The chordae tendineae were short and thick.

Within the left auricle there was a moderately firm, slightly oval, smooth-surfaced thrombus measuring 7×5 cm. A thin, recently formed post-mortem blood clot adhered to one edge of the thrombus and extended on to the ear of the auricle. After a careful search no small thrombi or areas of endocardial roughening were found. Upon section the central part of the thrombus was beginning to undergo softening, although as yet it was still compact.

Aorta: In the aorta from above the origin of the celiac axis and extending down for 2 cm. into the right iliac and 4 cm. into the left iliac artery there was a thrombus completely occluding this vessel. Sections taken through the aorta and iliac arteries showed the oldest part of the thrombus to be that in the left iliac artery and the lowermost portion of the aorta. The remainder probably is a propagated thrombus.

The uppermost part of the thrombus is smooth. The axillary arteries were opened from their beginning to a distance about halfway down the arm, but no thrombus was encountered. A probe passed further down met no resistance.

Lungs: No significant changes were found.

Spleen: The spleen was firm and presented one small depression, probably the result of a healed infarct.

Kidneys: The left kidney presented several deep depressions, probably the result of previous infarcts. The right kidney had several rather fresh infarcts with the typical yellowish area of necrosis and a zone of hemorrhage about it.

Pathological diagnosis.: (1) Free ball thrombus of the left auricle, (2) thrombosis of abdominal aorta, (3) mitral stenosis, (4) infarcts of kidneys and spleen, (5) chronic passive congestion of viscera.

COMMENT

In 1896, Von Ziemssen⁴ suggested for the first time, from a study of three patients, the possibility of diagnosing occluding auricular thrombi clinically. He stated that the criteria upon which the diagnosis could be made were: (1) absent or decreased pulsations in the peripheral vessels, (2) circumscribed gangrene of the feet, and (3) cadaveric coldness and swelling of the legs.

Since then, cases diagnosed clinically and confirmed by autopsy have been reported by Bozzolo⁵ in 1896, Lutembacher⁶ in 1917, Auberton and Rime⁷ in 1926, Covey, Crook, and Rogers¹ in 1928, Schwartz and Biloon² in 1931, and the one which we are presenting.

From examination of the case reports and the experience with the one presented by us, we are in accord with the opinion expressed by Schwartz and Biloon and others that the clinical diagnosis of a ball or pedunculated thrombus of the left auricle can be made and is justifiable under certain conditions. No conclusions could be drawn from the history alone, although the presence of a long-standing mitral stenosis together with auricular fibrillation, which were present almost invariably in the reported cases, adds somewhat to the possibility of this diagnosis. With a very few exceptions the signs over the heart itself are not unusual and do not aid us in determining the presence of this condition. The most important diagnostic feature, in our opinion, is the presence of the comparatively rapid and transitory changes in the peripheral circulation, such as marked cyanosis or even gangrene which may involve the finger tips, toes, or tip of the nose. Cadaveric coldness may occur suddenly, and quickly improve or disappear. The disappearance or diminution of pulsations, not from one extremity but from several of them, including both upper and lower, and their relatively rapid restoration as occurred in our case should be emphasized. Such symptoms cannot be explained on the basis of peripheral emboli alone. Moreover, it is unusual for peripheral thrombotic emboli to be given off to such wide-spread areas simultaneously. They can, however, be explained

by the presence of a ball thrombus in the left auricle which temporarily obstructs the flow of blood into the ventricle with consequent serious wide-spread impairment of peripheral circulation. With dislodgment of the thrombus, the symptoms and signs improve or disappear, the pulsations in the extremities return, the color becomes better, and the legs and arms become warm. These peripheral phenomena may be caused in two ways: (1) by obstruction of the mitral orifice with the ball thrombus, or (2) by the presence of emboli in the peripheral circulation together with the auricular ball thrombus, as occurred in the case we have described.

CONCLUSIONS

A case of free ball thrombus of the left auricle suspected ante mortem is presented, and the possibilities of making a diagnosis clinically are discussed.

The diagnosis is frequently impossible, but it can sometimes be made on the basis of (a) long-standing mitral stenosis usually with auricular fibrillation, and (b) wide-spread and transitory disturbances in the peripheral circulation.

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UNUSUAL MANIFESTATIONS FOLLOWING THE USE OF QUINIDINE SULPHATE IN A PATIENT WITH AURICULAR FLUTTER*

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THE following case of transient amblyopia and of an ectopic rhythm resembling ventricular tachycardia, following the administration of quinidine sulphate during the presence of auricular flutter, is of unusual interest.

REPORT OF CASE

B. G., a Jewish female, aged forty-five years, was admitted to the Montefiore Hospital on April 10, 1933, with a history of recurrent episodes of palpitation of the heart. Her heart rate varied between 110 and 220 beats per minute, and electrocardiograms revealed the underlying cardiac mechanism to be auricular flutter with a variable ventricular response. Congestive heart failure, such as enlargement of the liver and edema of the lower extremities, appeared when her heart rate remained elevated. Digitalis, administered in large doses, did not abolish this rhythm.

On April 19, 1933, two test doses of 0.2 gram each of quinidine sulphate were administered at a four hour interval. Following the second dose the patient complained of severe headache, dizziness, and nausea. The drug was then discontinued. She continued to show auricular flutter (Fig. 1-1). Digitalis was again given in 0.2-0.3 gram daily doses, but there was no effect on the heart rhythm. The paroxysms of 1:1 flutter continued unabated, and the condition of the patient became desperate.

On May 9, 1933, a probatory dose of 0.2 gram of quinidine was again given, and this time there were no toxic manifestations. A 0.2 gram dose of quinidine sulphate was then given every two hours for 8 doses on this day, and this dosage was repeated on the following day. The rate of the auricles persisted at 220 beats per minute, and the ventricular rate remained at 110 beats per minute. The total amount of the drug given on May 9 and 10 was 3.2 grams.

On May 11, 1933 (third day), after 6 similar doses had been given over a period of twelve hours, there was an increase in the ventricular rate to 204 beats per minute. The drug was then given every hour in the 0.2 gram doses until the following afternoon. At 2 P.M. of the next day (May 12, 1933) the flutter waves in the neck veins were no longer visible. The heart rate was 75 beats per minute. An electrocardiogram confirmed the presence of sinus rhythm with a marked increase in the P-R interval to 0.32 second (Fig. 1-2). The total amount of the drug given on May 11 was 3.6 grams.

The sinus rhythm persisted until 7 P.M. when, after slight exertion, there was a sudden rise in the heart rate to 180 beats per minute. The flutter waves were again seen in the neck. The hourly administration of quinidine, which had been discontinued one hour with the onset of sinus rhythm, was again resumed. The

*From the Medical Division of the Montefiore Hospital, Service of Dr. Leopold Lichtwitz.

ventricular rate now fell to 100 beats per minute but the rhythm was irregular, the irregularity being due to a variable ventricular response in the presence of auricular flutter. The total amount of the drug given on May 12 was 3.2 grams.

On May 13, 1933 (fifth day), only 5 doses of 0.2 gram of quinidine were given at two hour intervals. The administration of the drug was then discontinued for the day because numerous premature beats were observed in the electrocardiogram. The total amount of the drug given on May 13 was 1.0 gram.

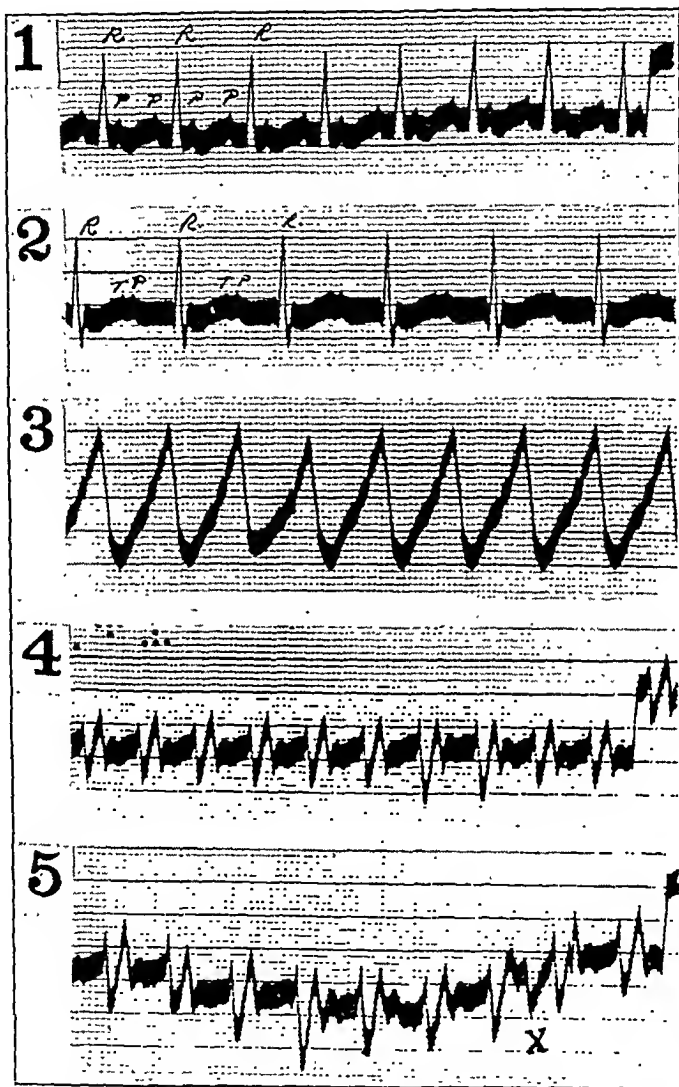


Fig. 1.—Lead I.

On May 14, 1933 (sixth day), the ventricular rhythm was again regular, the ventricles beating at 110 per minute and the auricles at 220. The patient received 0.2 gram of quinidine hourly for 4 doses, and then the interval between doses was increased to two hours. The total amount of the drug given on May 14 was 2.8 grams.

On May 15, 1933 (seventh day), the auricular flutter persisted, and the ventricular rate ranged from 80 to 110 beats per minute with a varying degree of block. During this day, however, multiple premature ventricular beats were again noted, and the

drug was temporarily discontinued after two doses of 0.2 gram each given at a two hour interval. The total amount of the drug given on May 15, was 0.4 gram.

On May 16, 1933 (eighth day), the ventricular rate ranged from 85 to 110 beats per minute, and the auricles still fluttered at a rate of 200 beats per minute until 2:30 P.M. when the ventricular rate suddenly increased to 220 beats per minute and the patient's pulse could not be felt. Quinidine sulphate was now again administered in 0.2 gram doses every hour. The ventricular rate fell to 100 beats per minute after two hours and remained at that level until late in the evening when there was another sudden rise to 200 beats per minute. Electrocardiograms at this time showed auricular flutter with a 1:1 ventricular response. The total amount of the drug given on May 16 was 1.8 grams.

On May 17, 1933 (ninth day), at 6 A.M. the degree of auriculoventricular nodal block increased, and the ventricular rate fell to 105 beats per minute. The patient was given hourly doses of 0.2 gram of quinidine sulphate. The ventricular rate remained at 100-110 until 8 P.M., when it again increased to 200 beats per minute. A 0.4 gram dose of quinidine sulphate was administered at hourly intervals for two doses, when the patient began vomiting; the drug was then discontinued. The total amount of the drug given on May 17 was 4.8 grams.

During that night the ventricular rate varied from 140 to 160 beats per minute and the patient went into circulatory collapse early the following morning.

On May 18, 1933 (tenth day), the respirations were Cheyne-Stokes in type; the lungs had filled up with moisture; and the ventricular rate persisted at 160 beats per minute and was regular. Metaphyllin solution, 2 c.c., was given intravenously with an immediate return to normal respirations. Early in the afternoon the patient regained consciousness. Later that afternoon she complained of inability to see. The fundi did not show any changes, and the neurological examination was also negative.

The electrocardiogram (Fig. 1-3) taken in the morning when the rate was 120 beats per minute showed an aberrant ventricular complex in the presence of a slow ventricular rate. However, the possibility of a ventricular response to every second auricular flutter impulse, with deformed ventricular complexes due to quinidine poisoning in the conduction mechanism in the ventricles must be considered, especially in the light of later records. At 2 P.M. the ventricular rate was 149 beats per minute and regular (Fig. 1-4). This record shows the aberrant nature of the ventricular complexes to be less marked than in previous records. (No quinidine sulphate was given on May 18.)

Two hours later another record (Fig. 1-5) disclosed the same type of ventricular complex as in Fig. 1-4. However, there was a definite irregularity in the rhythm due to an interpolated ventricular beat (Fig. 1-5X) which resembled the other ventricular complexes in this lead. The ventricular rate is doubled by the interpolation of this beat. This is further evidence that we may be dealing here with an auricular flutter with a 2:1 response interrupted in this one instance by a 1:1 response of auricle to ventricle. The aberrant nature of the ventricular complexes may be due to quinidine intoxication, since they disappeared after quinidine was discontinued. However, we cannot definitely rule out the possibility of an ectopic ventricular tachycardia.

Subsequent Course.—The ventricular rate on the evening of May 18, 1933 (tenth day), again increased to 180 beats per minute and throughout the night ranged from 180 to 220 beats per minute. No quinidine sulphate had been given this day. The patient again went into circulatory collapse. Early the next morning (May 19) the ventricular rate fell to 100-120 beats per minute, and the patient's condition im-

proved. Later that day she could dimly see moving objects. Toward evening a left homonymous hemianopsia was found. On the following day (May 20) the patient's visual fields became larger and gradually increased until they again were normal. The ventricular rate remained at 100-120 until May 23, when moderate doses of digitalis were again administered and fibrillation of the auricles resulted, although digitalization before the quinidine sulphate had been administered had not altered the rhythm. The ventricular rate was now maintained at 80-100 beats per minute by the administration of large daily doses of this drug for four weeks, when the paroxysms of 1:1 flutter returned at irregular intervals.

SUMMARY

A woman with hypertension and repeated paroxysms of 1:1 auricular flutter received 20.8 grams of quinidine sulphate within nine days, in total doses ranging from 0.4 gram to 4.8 grams a day with the purpose of abolishing this abnormal rhythm.

The doses ranged from 0.2 gram of the drug at two hour intervals to 0.4 gram at hour intervals. On the fourth day, after 9 grams of quinidine had been administered, the auricular flutter was temporarily abolished and normal sinus rhythm was restored for a few hours. Following the reestablishment of auricular flutter, the patient went into circulatory collapse on several occasions when there was a return of the 1:1 flutter.

A ventricular rhythm with widely aberrant complexes resembling those seen in ectopic ventricular tachycardias was found on the ninth day, and the drug was then discontinued. All these abnormal complexes then disappeared. On the tenth day, one day after the drug had been discontinued, the patient complained of blindness which gradually disappeared, and normal vision returned after four days.

Department of Reviews and Abstracts

Selected Abstracts

Simmons, Stanley T.: Rheumatic Heart Disease: Clinical Data as Observed in Louisville, Kentucky. *Am. J. M. Sc.* 187: 773, 1934.

In this study of 206 cases of rheumatic heart disease seen in the Louisville City Hospital, it was noted that the disease occurred most commonly in the third and fourth decades of life. The sex incidence showed the usual greater frequency of infection in females in the ratio of 3:2. There was a predominance of white patients to colored in the ratio of 5:3. There was a definite history of rheumatic infection in 91 per cent; 68 per cent of the patients had had rheumatic fever. The first attack occurred before the age of thirty years in 93.5 per cent. The primary infection occurred in only one patient after the age of forty. Seventy-five per cent of the patients were in the hospital some time during the period covered by the study with cardiac symptoms. Eighty-five per cent showed some degree of decompensation before the fortieth year.

Weinstein, A. A.; Davis, David; Berlin, D. D.; and Blumgart, H. L.: The Mechanism of the Early Relief of Pain in Patients With Angina Pectoris and Congestive Failure After Total Ablation of the Normal Thyroid Gland. *Am. J. M. Sc.* 187: 753, 1934.

Observations on the immediate postoperative relief of chest pain after total thyroidectomy in nineteen patients are described.

Data were collected before, immediately after, and during several weeks after operation in three groups: (1) changes in nonanginal precordial pain; (2) changes in areas of skin hyperesthesia and muscle and periosteal hyperalgesia of the chest wall; (3) changes in the character and distribution of pain of angina pectoris.

Within a few hours after operation, nonanginal precordial pain, hyperalgesia, and hyperesthesia disappeared, remained absent from two to four weeks but then usually reappeared if the basal metabolic rate had not declined significantly. Only after the basal metabolic rate had dropped appreciably did the above mentioned signs and symptoms diminish or disappear permanently.

Studies were made on the distribution of the pain of angina pectoris produced under standard conditions in three patients before and after hemithyroidectomy. The remaining half of the thyroid gland was removed at a later date. Exercise within two weeks after hemithyroidectomy produced no pain in the arm and the side of the chest corresponding to the side of operation. The pain of angina pectoris was experienced only on the unoperated side and usually stopped sharply at the midline of the sternum. The similarity of these findings to those after cervical sympathectomy and alcohol injection is discussed. The basal metabolic rate did not change appreciably after the first hemithyroidectomy. After from two to eight weeks, pain on exercise was again experienced on the operated side.

Only after removal of the other half of the thyroid gland and after an appreciable drop in the basal metabolic rate was the pain of angina pectoris permanently relieved.

These observations point definitely to the following conclusions: (1) the immediate relief of pain after total thyroidectomy is due to the interruption of afferent nerve impulses from the heart at the time of operation; (2) relief by this mechanism is only temporary; (3) permanent relief is related to the lessened work of the heart attendant on the development of the hypothyroid state.

These findings indicate that after total ablation of the thyroid, complete bed rest should be enforced, despite the early subjective relief experienced by the patient, until the basal metabolic rate shows significant lowering.

Stroud, William D.; Bromer, Albert W.; Gallagher, J. Roswell; and Vander Veer, Joseph B.: *A Clinical Comparison of a Purified Glucoside and Whole Leaf Preparations of Digitalis*. *Am. J. M. Sc.* 187: 746, 1934.

The present study was undertaken in an effort to determine whether or not there is any difference in the therapeutic value of whole leaf as compared with a purified glucoside preparation of digitalis. Twenty-five ambulatory cases of established auricular fibrillation were divided into three similar groups. One group was given a preparation of the extracted, purified glucosides of digitalis; another was given a whole leaf preparation manufactured by a well-established pharmaceutical house; and the third group received whole leaf tablets prepared by the American Heart Association. The groups were followed clinically for nine months and then, after interchanging the preparations, for another period of six months. No significant difference could be ascertained in the clinical pictures of the patients in the three groups during the period of observation.

The Etiology of Acute Rheumatism and Chorea in Relation to Social and Environmental Factors. Joint Discussion of the Section on Epidemiology and Section for the Study of Disease in Children. *Proc. Roy. Soc. Med.* 27: 953, 1934.

This discussion by various speakers presents briefly the current ideas on the etiology of rheumatism and chorea in relation to many social and environmental factors. It summarizes briefly, especially the English viewpoint, the many obscure and debatable points in connection with this disease. Several important observations not otherwise reported are included in the discussion.

Pomerance, Max, and Frucht, Simon: *Heart Block in Rheumatic Fever*. *Am. J. Dis. Child.* 47: 1087, 1934.

In a series of children with rheumatic fever, thirty-one in number, twenty-eight showed prolongation of the P-R interval; the other three showed complete dissociation, complete heart-block and left bundle-branch block, occurring during the acute attack. These three cases illustrate four important considerations of these disturbances of cardiac rhythm: (1) the fleeting character of the abnormal rhythm; (2) the accelerated ventricular rate in complete heart-block, making the clinical diagnosis impossible; (3) the curious auriculoventricular dissociation in which the ventricular rate is higher than the auricular rate; (4) the necessity for exact records in all rheumatic cases.

Siemsen, Walter J.: *Evaluation of Nonorganic Auscultatory Cardiac Findings and the Venous Hum in Children*. *Am. J. Dis. Child.* 47: 1100, 1934.

Healthy boys attending the University of Chicago laboratory schools and ranging in age from five to eighteen years served as subjects for the observations reported. Except for the exclusion of children with abnormal cardiac findings

or with physical incapacitation and except for the omission of cases because of incomplete data, the material was unselected. Observations were made during the routine annual examinations, the boys thus being unaware of any unusual proceedings. Observations were made on the incidence of arrhythmias, the incidence of third heart sounds, reduplicated heart sounds, functional heart murmurs, murmurs produced by exercise, and the venous hum.

On the basis of the evidence accumulated, the author attempts to point out the insignificance of presumably nonorganic auscultatory cardiac findings as commonly encountered. While the inconsequential nature of the phenomena has been stressed, emphasis on due care in their proper evaluation has been omitted.

Neiman, Benjamin H.: Verrucous Aortitis With Special Regard to Aneurysm Formation in Children. J. Lab. & Clin. Med. 19: 929, 1934.

In a series of 4,100 consecutive autopsies, 3 cases have been found in which there was a verrucous lesion on the intima of the aorta. In one case which was associated with a stenosis of the isthmus, the verrucous aortitis had caused a spontaneous rupture of the aorta in an eleven-year-old child. In another, a four-year-old child, an aneurysm of the aorta developed on the basis of it and ruptured into the pericardial sac. Streptococci were demonstrated in this case.

The formation of the verrucae is explained on the basis of a fibrinoid swelling and necrosis of the ground substance of the intima with proliferation of the adjacent fibrocytes. The rupture and aneurysm are explained on the basis of necrosis destroying the internal elastic membrane with subsequent weakening of the media. The nonspecificity of the verrucous lesion of the intima of the aorta is pointed out.

Friedberg, Charles K., and Gross, Louis: Periarthritis Nodosa (Necrotizing Arteritis) Associated With Rheumatic Heart Disease. Arch. Int. Med. 54: 170, 1934.

Four cases that came to autopsy are presented in which widespread periarthritis nodosa was associated with rheumatic fever and rheumatic heart disease; the latter was confirmed by the presence of Aschoff bodies in the myocardium. These four were discovered in a series of eight cases of periarthritis nodosa which came to autopsy in the course of two years. Prior to this period there were five additional cases which came to autopsy. Two of the five patients had a rheumatic history and evidence of rheumatic valvular disease. Verrucous endocarditis was disclosed in both cases at postmortem examination.

Criteria for the diagnosis of rheumatic infection and of periarthritis nodosa are discussed. On the basis of these criteria, none of the cases of periarthritis reported in the literature presented adequate evidence of rheumatic heart disease. Conversely, none of the vascular lesions described in rheumatic fever could be truly called periarthritis nodosa. Because of the frequency of the association of these diseases in this series and the simultaneous occurrence of the symptoms of each, it is believed that rheumatic fever is probably a common cause of the vascular lesions termed periarthritis nodosa.

In two of the cases an attack of scarlet fever occurred eight weeks before the symptoms of the other ailments became manifest. This point is briefly discussed. In another case there was clinical and pathological evidence of malignant sclerosis. This is mentioned in connection with Fahr's belief that rheumatic fever is one of the causes of malignant sclerosis. In two of the cases the abdominal symptoms, so common in periarthritis nodosa, dominated the clinical picture sufficiently to lead to an exploratory operation. It is suggested that when acute abdominal symptoms

are present in a patient suffering from rheumatic fever, complicating periarteritis nodosa should be considered. This complication is offered as an organic basis for some of the instances of so-called abdominal rheumatism.

Campbell, Maurice: The Respiratory Exchange During Exercise in Heart Disease.
Quart. J. Med. 3: 369, 1934.

In patients with heart disease, the percentage increase of the pulmonary ventilation during easy exercise was normal. The increase took place more slowly at the beginning and lasted longer afterward. At rest the ventilation was rather greater relatively to their size, and this remained true during and after exercise.

The breathing was faster and more shallow, especially during exercise. This rapid shallow breathing was more characteristic of mitral stenosis and of those who were most breathless. The effective alveolar ventilation was therefore a smaller percentage of the total pulmonary ventilation. Both these factors would tend to cause dyspnea, but alone they would not do so in a normal subject.

In spite of the shallow breathing the percentage of the vital capacity which was needed, even during these easy exercises, was greater than normal (33 against 20 per cent). No doubt this was an important factor in the sensation of breathlessness.

The percentage of carbon dioxide in the expired air was lower than normal, and this difference was increased during exercise, especially in those with mitral stenosis, and in those who were short of breath with easy walking.

The output of carbon dioxide, especially in the first minute of exercise, was less than normal, and this lag would be responsible for some degree of hyperpnea during the remainder of the exercise and after. The utilization of oxygen was almost the same as normal, and the oxygen debt at the end of exercise was less than this retention of carbon dioxide. The pulmonary ventilation and the intake of oxygen did not differ greatly from the normal in these patients with heart disease.

It seems probable that the more rapid shallow breathing with a smaller effective alveolar ventilation and the lower percentage of carbon dioxide expired were factors in the production of their dyspnea. But the smaller margin between their depth of breathing and their maximum vital capacity appeared a more important factor in their sensation of dyspnea.

Gilchrist, A. Rae: The Effects of Bodily Rest, Muscular Activity and Induced Pyrexia on the Ventricular Rate in Complete Heart Block. Quart. J. Med. 3: 381, 1934.

The ventricular rate in complete heart-block is not fixed but under conditions of bodily rest fluctuates through a range of rate more or less peculiar to the individual.

Clinically it was possible to divide these cases into broad groups—a degenerative and a "toxic" variety. The coefficient of correlation between the auricular and the ventricular rates is less perfect in the "toxic" than in the degenerative group, indicating a more labile regulation of the independent rhythms in the former.

Muscular exercise increases the rate of ventricular beating in complete heart-block. A simple test, consisting of repeatedly climbing a height of 1.5 feet in a given time, induced a maximum increase of 50.2 beats per minute in one patient and a minimum of 1.2 beats in another. The power to increase the rate of ventricular beating in response to exertion varies considerably in different individuals. Similarly the rate of the recovery process is inconstant. In some patients the ventricles return to their preexisting rate within one minute of completing the test; in others three, four or five minutes may elapse before the rates become fully readjusted to resting conditions.

The maximum natural range in auricular and ventricular rates has been estimated by taking the difference between the rate recorded immediately after exercise and the minimum rate observed in a series of observations for each individual under conditions of prolonged bodily rest. The maximum range in rate varies in different subjects, and the maximum auricular and ventricular ranges are not of the same order of magnitude.

In this series of cases it is found that the maximum auricular and ventricular ranges vary inversely. A range of 150 per cent in auricular rate is accompanied by only 10 per cent in ventricular; a 50 per cent gain in auricular rate coexists with a 100 per cent gain in ventricular. In other words, the greater the limitation in ventricular range the more labile the auricular. The greater the ventricular range the less incapacitating are the cardiac symptoms. In complete heart-block an important factor in promoting myocardial efficiency is the ability to quicken the ventricular rate in response to the demands of physical exertion.

In three patients it was found that during sleep the ventricular rate was slower than that recorded under similar conditions awake.

Fever increases the rate of ventricular beating in complete heart-block. In the course of the "protein-shock" reaction a rise of 1° F. may account for an increase of about four beats per minute in the rate of the ventricles.

These observations suggest that functionally there is no essential difference between the sino-auricular node and the idioventricular center. Each reacts to similar forms of stimulation, but the magnitude of the responses would appear to be limited chiefly by the natural differences in the rhythmicity of the two centers of impulse production.

Richards, Dickinson W., and Barach, Alvan L.: Prolonged Residence in High Oxygen Atmospheres. Effects on Normal Individuals and on Patients With Chronic Cardiac and Pulmonary Insufficiency. Quart. J. Med. 3: 437, 1934.

Two normal men and twenty-eight patients in the cardiac insufficiency state have been kept in atmospheres of from 40 to 50 per cent oxygen for continuous periods ranging in length from five days to seven months. Studies have been made in these subjects, of the effects of high oxygen atmospheres upon circulatory and pulmonary functions, and in certain instances upon their water and electrolyte balances.

Two normal subjects residing for a week in 45 per cent oxygen showed a fall in pulse rate, a slight rise in blood CO₂ levels, no appreciable change in respiratory metabolism, in cardiac output, or in excretion of electrolytes or water.

The response to high oxygen atmosphere in favorable cases of congestive heart failure was found to follow a fairly definite pattern or sequence of events.

(a) Dyspnea and restlessness were partly relieved within a few hours, but completely relieved only after several days.

(b) Arterial oxygen saturation was restored to normal or raised slightly above normal within the first twenty-four hours. Rise in blood CO₂ began on the first day, then continued progressively for several days.

(c) Increase in urinary chloride and water excretion frequently occurred, beginning from one to six days after the beginning of oxygen treatment, then proceeding to complete loss of edema.

The favorable response to prolonged oxygen treatment was found to be similar in general course to the recovery of compensation by other means, though definite differences in certain details were encountered. These have been further discussed.

Of twelve cases of arteriosclerotic heart disease, severely decompensated, eight patients were restored to limited ambulatory activity, following prolonged oxygen

treatment, three were temporarily improved, one was not improved. Eight out of nine patients with edema had a diuresis during their course in high oxygen.

Of nine patients with rheumatic heart disease severely decompensated, none was restored to ambulatory activity. Five patients showed moderate improvement and relief of symptoms; the remaining four were not appreciably improved.

Of five patients with pulmonary fibrosis with secondary circulatory insufficiency, all were improved. Two were restored to ambulatory activity.

The clinical indications for oxygen therapy in relative order of importance, are: (a) dyspnea; (b) restlessness; (c) cardiac pain of anginal type; (d) arterial oxygen unsaturation; (e) cyanosis; (f) cough.

Cowan, Donald W.: The Creatine Content and the Weight of the Ventricles in Experimental Hyperthyroidism and After Thyroparathyroidectomy. *Am. J. Physiol.* 109: 312, 1934.

The present investigation was undertaken to determine the effect of both hyper- and hypothyroidism upon the creatine concentration as well as the total amount of creatine in the ventricles of experimental animals. Young adult male rats were used in this work.

Thyroxine whether administered in divided doses over a period of time or in a single large dose causes an actual increase in ventricular muscle mass (in spite of a lowering of general body weight). There is a decrease in creatine concentration in the ventricles and an actual loss of creatine from the heart.

Thyroparathyroidectomy while producing no change in the weight of the ventricles does cause a slight but significant loss of creatine from the heart.

Nathanson, M. H.: Further Observations on the Effect of Drugs on Induced Cardiac Standstill. *Arch. Int. Med.* 54: 111, 1934.

In certain persons the activity of the cardiac pacemaker may be temporarily eliminated and an arrest of the heart induced by pressure on the right carotid sinus. In eight cases studied, the subcutaneous injection of epinephrine abolished the standstill by stimulating a new center of impulse formation in the ventricles. Ephedrine administered intravenously produced a similar response in three cases. Barium chloride by mouth abolished the cardiac standstill in a similar manner in one case and was ineffective in another. Calcium gluconate, caffein sodium benzoate, coramin metrazol and thyroxine were without effect in a subject who responded consistently to epinephrine. Digitalis prolonged the period of induced cardiac standstill. A group of compounds chemically related to epinephrine produced in a varying degree a reaction similar to that of epinephrine. The ratio of activity of these compounds as compared with epinephrine was estimated.

The effectiveness of the epinephrine-like compounds indicates that in the therapy of cardiac standstill a specific pharmacodynamic action is required, which is the stimulation of the cardiac accelerator mechanism.

Epinephrine is the most active drug in the treatment of the stopped heart and in the prevention of the frequent syncopal attacks of chronic heart-block.

Harrison, T. R.: Friedman, Ben; Clark, Gurney; and Resnik, Harry: The Cardiac Output in Relation to Cardiac Failure. *Arch. Int. Med.* 54: 239, 1934.

The cardiac output of patients with cardiac disease has been studied by the acetylene method, modified in such a way as to allow the detection of inaccurate results. The cardiac output per minute of patients with congestive heart failure

is usually from 10 to 30 per cent less than that of normal subjects but may be within the normal range. Patients without circulatory disorders may have an equally low cardiac output. The level of the cardiac output per minute, whether considered as such or in relation to the metabolic rate, bears no relation to the presence or absence of congestive failure for:

1. The range and the average values of the cardiac output are similar for compensated and decompensated patients.

2. In a given individual, clinical improvement and disappearance of congestive phenomena may be associated with an increase, a decrease or no change in this function. In general, the output of the heart per beat tends to be somewhat less during congestive failure. The metabolic rate is normal in some patients and elevated in others.

These observations are interpreted as indicating that the "forward failure" (diminished output) hypothesis, which ascribes the clinical manifestations of congestive heart failure to an insufficient supply of blood to the tissues, is erroneous. The "backward failure" (back pressure) theory has been discussed, and it is concluded that there is much evidence in favor of it and no valid evidence against it.

Thompson, H. E., and Dragstedt, C. A.: Modifying Action of Calcium and Sodium Bicarbonate of Salicylate Intoxication. Arch. Int. Med. 54: 308, 1934.

Experiments on normal healthy dogs were undertaken to determine whether a mixture of calcium salt with acetyl salicylic acid would be less toxic than acetyl salicylic acid alone. The amount of the drug used was large enough to correspond to an intensive type of salicylate medication employed clinically for short periods to accomplish what may be called salicylization.

The ameliorating effect of sodium bicarbonate on certain of the untoward symptoms produced by salicylate medication in these amounts reported by many workers is confirmed by these experiments. Simultaneous administration of calcium in the form of calcium gluconate and acetyl salicylic acid was found to have a similar and in certain respects, a greater ameliorating effect.

Meeker, Dorothy R., and Jobling, James W.: A Chemical Study of Arteriosclerotic Lesions in the Human Aorta. Arch. Path. 18: 252, 1934.

Analysis of arteriosclerotic plaques after careful isolation of the portions involved in intimal lesions apart from other portions of the aorta from forty-five patients showed a constant amount of phospholipids, an increase of total fatty extract and total cholesterol particularly in the proportion of cholesterol to total fatty extract. This increase apparently becomes greater with increasing severity in the lesions rather than with increasing age. The study also showed that as the severity of the lesions increases, there is first an increase in percentage of cholesterol esters, in a fatty extract and then as the process continues, a decrease.

Bellet, Samuel, and Johnston, Charles G.: The Effect of Coronary Occlusion Upon the Initial Phase of the Ventricular Complex in Precordial Leads. J. Clin. Investigation 13: 725, 1934.

In acute experiments upon dogs and cats ligation of the anterior descending branch of the left coronary artery, while causing R-T deviation in precordial leads, produced practically no change in the initial downward deflection of the ventricular complex. In general, ischemia or damage to a much greater portion of the myocardium than that supplied by the anterior descending branch of the left coronary artery was required to produce a marked diminution or disappearance of the initial downward deflection. Diminution or disappearance of this deflection was produced in cats

after ligation of the anterior branch of the left coronary plus the anterior branch of the circumflex arteries, or in dogs and cats after cauterization of a considerable portion of the surface of the cardiac muscle.

In survival experiments marked diminution or disappearance of the initial downward deflection could be produced by ligation of the anterior descending branch of the left coronary artery alone. In 3 out of 5 dogs this deflection almost completely disappeared from twenty-four to forty-eight hours after ligation. In one cat it disappeared two hours after operation. In one dog it was markedly diminished on the fifth day after operation and in another moderately diminished on the third day. In all 5 dogs, later during the recovery stage, it increased again; in one instance the return was complete; in the remaining 4 the deflection regained one-fourth to one-half its original amplitude. In man the initial downward deflection which disappears during the acute stage of infarction usually does not return in the chronic stage; occasionally, however, a partial return occurs. The return of this deflection in the dog is probably to be explained by the smaller relative size of the area involved by the chronic infarct and by the larger portion of the left ventricle in relation with the anterior chest wall in the dog.

Extremely tall T-waves observed in these experiments as a transient phenomenon are believed to characterize a subacute stage of infarction.

Ligation of the coronary arteries supplying the posterior wall of the left ventricles or injury of this area by cauterization produced R-T interval deviations above the isoelectric line but no change in the amplitude of the initial downward deflection.

Gilligan, D. R.; Berlin, D. D.; Volk, M. C.; Stern, B.; and Blumgart, H. L.: Therapeutic Effect of Total Ablation of Normal Thyroid on Congestive Heart Failure and Angina Pectoris. IX. Postoperative Parathyroid Function. Clinical Observations and Serum Calcium and Phosphorus Studies. *J. Clin. Investigation* 13: 789, 1934.

Tetanic convulsions or spontaneous spasm of the extremities did not occur in any of the seventy-three consecutive patients on whom total thyroidectomy was performed. Clinical signs or symptoms of mild parathyroid deficiency were manifest after operation in twelve patients, or 17 per cent, of this entire series. Of the last thirty-seven patients of this group of seventy-three, only three, or 8 per cent, showed signs or symptoms. In ten of the twelve patients clinical signs and symptoms of hypoparathyroidism were transient, disappearing within two weeks. One patient who was operated upon two and a half months previously and another nine months previously still showed signs and symptoms when specific medication was discontinued. The symptoms of hypoparathyroidism are attributed to injury, rather than to removal of parathyroid glands during operation.

Oral administration of calcium chloride solution and a diet rich in milk controlled the symptoms of tetany in most patients in whom the disease was transient. An initial intravenous injection of calcium chloride solution was given to three patients; calcium lactate or gluconate was substituted when oral administration of calcium chloride solution was not tolerated. Viosterol, together with a large intake of calcium, is being employed successfully in the two cases with persistent hypoparathyroidism.

The serum calcium was reduced to 7.5 mg. per 100 c.c. or less in six of the twelve cases at the time of onset of tetany; in three cases the serum calcium was between 8.3 and 8.6 mg. per 100 c.c.; in the remaining three cases the serum calcium was within the accepted normal limits. The values for serum inorganic phosphorus in these patients with early postoperative tetany were usually normal, being 5.0 mg. per cent or above in only two cases.

Appreciable decreases in concentration of serum calcium and no changes in concentration of serum inorganic phosphorus were observed during the first two weeks after total thyroidectomy in a group of patients who showed no clinical signs of insufficient parathyroid function. The concentration of serum calcium was usually slightly below the preoperative level during the first year after thyroidectomy, both in those individuals who showed transient signs and symptoms of hypoparathyroidism soon after operation and in patients who showed no clinical signs of this disorder at any time.

It is pointed out that the chemical changes in the blood present during the early stages of postoperative tetany may be quite different from the characteristic markedly low serum calcium and high phosphorus values found in chronic hypoparathyroidism of either idiopathic or postoperative origin.

The transient tetany which sometimes occurs immediately following total thyroidectomy can be controlled by calcium therapy; persistent parathyroid insufficiency occurs so rarely that it does not constitute a contraindication to total thyroidectomy.

Pwelow, S., Markle, P., and Katz, L. N.: Factors Involved in the Production of Skeletal Muscle Pain. Arch. Int. Med. 53: 814, 1934.

The results of this study show that the immediate cause of continuous muscular pain such as occurs when an ischemic muscle is exercised is not produced by a single mechanism but that muscular activity, anoxemia, circulatory stasis and possibly other processes contribute to its production.

Ernstene, A. Carlton, and Snyder, Maurice: Effect of Arteriosclerosis and Benign and Malignant Hypertension on the Area of Histamine Flares. Arch. Int. Med. 53: 865, 1934.

The area of flare produced by injecting 0.02 c.c. of a 1:2,000 dilution of histamine dihydrochloride into the skin of the mid forearm was measured in five groups: normal persons, patients with arteriosclerosis and normal blood pressure, patients with benign essential hypertension, patients with hypertension of the intermediate grade, and patients with malignant hypertension. In eleven of the sixteen patients with malignant hypertension, the area of flare was less than the smallest recorded in a normal person, while in only three did it exceed 24 sq. cm. The average area for the group was 16 sq. cm., approximately one-half that of normal persons.

The results of the investigation indicate that observations on the area of the histamine flare should prove a useful adjunct in distinguishing the intermediate and malignant types of hypertension from the benign form.

Allen, Edgar V., and Camp, John D.: The Value of Arteriography. Radiology 22: 678, 1934.

The roentgenographic studies in a case of thromboangiitis obliterans indicate not only the diagnostic value of arteriography but also the powers of compensation for disease which are inherent in the arterial system.

The chief value of arteriography in the authors' estimation lies not in the direction of diagnoses but in determining the pathogenesis of the condition. It gives information of inestimable value regarding the disturbances in the arterial circulation in scleroderma, thromboangiitis obliterans, in aneurysms, arteriovenous fistulas and arterial emboli. Whether or not the method will add information of value to knowledge of pathogenesis of arthritis, hypertension and of other conditions remains to be learned in the future.

Clark, Janet H., Hooker, Donald R., and Weed, Lewis H.: The Hydrostatic Factor in Venous Pressure Measurements. *Am. J. Physiol.* 109: 166, 1934.

Direct measurements of the venous pressure in dogs in the horizontal and two vertical (head-down, head-up) positions have shown that the heart is not the point from which the hydrostatic factor in venous pressure is measured. In the dead animal the venous system acts as an unbroken column from head to tail, and the reference point from which hydrostatic pressure is measured was found to be 82 mm. caudal to the heart in the vertical position in an animal of approximately 500 mm. spinal length. In the living animal the venous system is broken at the heart, giving two columns with a reference point approximately 121 mm. from the heart in the tail section and another reference point 38 mm. from the heart in the head section.

Kovacs, Joseph: The Iontophoresis of Acetyl-Beta-Methylcholin Chlorid in the Treatment of Chronic Arthritis and Peripheral Vascular Disease. *Am. J. M. Sc.* 188: 32, 1934.

A preliminary report on the action of the iontophoresis of acetyl-beta-methyleholin chlorid is presented.

Acetyl-beta-methyleholin chlorid introduced locally with the help of the galvanic current produces a pronounced and prolonged local effect which cannot be obtained through subcutaneous or oral administration. This local treatment appears to be of value in chronic arthritis especially in the rheumatoid type. This treatment may also be of value for patients with peripheral vascular disease in which spasm is an important factor. No harmful effects were observed.

Further studies with prolonged observation of cases, especially in view of the fallacies lurking in the evaluation of the therapeutic test, are essential for the correct evaluation of this method.

Bruen, Curtis: The Therapeutic Efficacy of Bismuth Subnitrate in Arterial Hypertension. *Am. J. M. Sc.* 188: 21, 1934.

Under the conditions established for experimental observation, it was determined that bismuth subnitrate by mouth even in the largest therapeutically practicable doses does not develop sufficient nitrate action to exert any demonstrable effect on the blood pressure or symptoms of arterial hypertension.

Nadler, J. Ernest; Green, Henry; and Rosenbaum, Arthur: Intravenous Injection of Methylene Blue in Man With Reference to Its Toxic Symptoms and Effect on the Electrocardiogram. *Am. J. M. Sc.* 188: 15, 1934.

These observations indicate that methylene blue under the conditions of this study has two actions. The first of these is the oxidation of hemoglobin to methemoglobin. The amount of methemoglobin found immediately following the injection of the average therapeutic dose is small.

The second is that this drug, used intravenously, excites the individual and by its rapid elimination into the stomach and urine produces transitory gastrointestinal and urinary irritation. The most frequent toxic symptoms observed were restlessness, paresthesias, a sense of "burning" in the mouth and stomach, pain in the chest, and strangury. These manifestations usually subsided in from twenty-four to forty-eight hours. Leakage of a small amount of methylene blue about the vein gives rise to a very painful infiltration.

Electrocardiographic studies show that methylene blue produces a reduction in the height or even reversal of the T-wave frequently with lowering of the R-wave. This suggests depression of the ventricular musculature.

The amount of methemoglobin found and the subsequent decrease in hemoglobin is not of sufficient magnitude to account for the clinical picture described on the basis of anoxemia.

The authors wish to point out, therefore, that the indiscriminate use of methylene blue may produce unpleasant results and be dangerous to the patient.

Harrison, T. R.; King, C. E.; Calhoun, J. A.; and Harrison, W. G., Jr.: Congestive Heart Failure. XX. Cheyne-Stokes Respiration as the Cause of Paroxysmal Dyspnea at the Onset of Sleep. *Arch. Int. Med.* 53: 891, 1934.

A pneumographic study has been made of patients complaining of attacks of dyspnea coming at the onset of sleep. Such patients exhibit Cheyne-Stokes respiration which either appears or becomes more marked at the onset of sleep and later during deep sleep either disappears or becomes less marked. As sleep develops, respiratory periodicity occurs with increasing length of the apneic intervals and a corresponding increase in the intensity of the hyperpneic phase, which eventually becomes so marked as to awaken the patient and cause dyspnea.

An investigation has been made concerning the underlying factors responsible for these phenomena, and it is concluded that the main causative agents are: over-ventilation due to reflex respiratory stimulation from congested lungs and respiratory depression occurring at the onset of sleep. Acting singly or in combination, these two physiologic alterations appear to be responsible for the periodic breathing. The associated violet hyperpnea in a patient with diminished vital capacity is responsible for the subjective respiratory distress.

Certain observations on the blood gases before and during sleep have been presented, and these are compatible with the hypothesis mentioned. The development of periodic breathing is usually not associated with significant alterations in the composition of the blood. As sleep continues there is, however, a demonstrable increase in the carbon dioxide tension and in the acidity of the blood, and coincidentally the respiration becomes regular.

The alterations in the blood gases are primarily effects of the changes in breathing. However, as a result of the alteration in the blood, the breathing undergoes further changes which lead to the production of the characteristic paroxysmal seizures of respiratory distress.

Friedman, Ben, Clark, Gurney, and Harrison, T. R.: Studies in Congestive Heart Failure. XXII. A Method for Obtaining "Mixed" Venous Blood by Arterial Puncture. *J. Clin. Investigation* 13: 533, 1934.

A modification of the method of Burwell and Robinson for determining the gas contents of "mixed" venous blood has been described. The procedure depends on obtaining blood from a peripheral artery while the subject breathes a gas mixture which has been equilibrated with his venous blood by previous repeated rebreathings.

The several procedures involved in the method have been checked by various experiments.

Application of the method to dogs has demonstrated that the values found for the blood gases by this indirect method are in close agreement with the gas contents of blood obtained by puncture of the right ventricle. The presence in the lungs of sufficient fluid to produce well-marked arterial anoxemia does not invalidate the results.

The method is difficult to employ and involves considerable discomfort to the subject. Its agreement with the modified acetylene procedure constitutes additional evidence as to the validity of the latter in subjects with cardiac disease.

Harrison, T. R., Calhoun, J. A., and Harrison, W. G., Jr.: Congestive Heart Failure. XXI. Observations Concerning the Mechanism of Cardiac Asthma. *Arch. Int. Med.* 53: 911, 1934.

Cardiac asthma has been defined and has been differentiated from other types of paroxysmal and nocturnal dyspnea occurring in patients with cardiac disease. The dyspnea of cardiac asthma is not usually associated with abnormalities in the oxygen, carbon dioxide or hydrogen ion content of the arterial blood.

Relief of the seizure of morphine is not associated with constant alteration in the gases of the blood but is followed by a decrease in ventilation and is usually accompanied by an increase in vital capacity.

Pulmonary congestion, with its twofold effect of decrease in vital capacity and reflex respiratory stimulation, is always present and appears to be the underlying cause of cardiac asthma.

There are a number of different precipitating causes of the seizures. Of these, cough is the most common. Less frequently, fear—produced by unpleasant dreams—abdominal distention or warmth may precipitate the seizures. Each of these precipitating factors appears to act by increasing the ventilation. It has been shown that, both in normal persons and in patients with cardiac disease, an increase in ventilation is accompanied by a rise in consumption of oxygen, which occurs immediately and thereby indicates that the cardiac output is also increased.

The effects of voluntary overventilation on the vital capacity were studied in normal subjects and in patients with left ventricular failure. The former persons usually had a slight rise in vital capacity, but the reverse effect was usually obtained in the patients.

A typical seizure of cardiac asthma was produced in one patient by voluntary overventilation and in another subject by voluntary coughing.

Acute pulmonary edema causes both chemical and reflex stimulation of breathing and may thus accentuate dyspnea. It has also been shown that in dogs "edema" of the lungs produced by introducing Ringer's solution may cause marked anoxemia with a consequent increase in the cardiac output.

It has been shown that patients dying with congestion of the lungs may have a noninflammatory edema of the bronchial walls, and this is believed to be responsible for the musical and sonorous râles which are often heard during the dyspneic seizures. Thus, an "obstructive" dyspnea may be superimposed on a "reflex" dyspnea.

The occurrence of the attacks during sleep appears to be dependent on the depressed irritability which allows the various stimuli mentioned to become excessive before they awaken the patient. On awakening there is marked increase in breathing because of the sudden increase in irritability of the respiratory center, plus the strong stimulus. The resulting increase in ventilation tends to cause additional pulmonary congestion which leads to further increase in ventilation. The vicious cycle so started may progress to acute pulmonary edema unless it is broken by the patient's assuming the upright posture, by the administration of morphine or by removal of the precipitating cause, i.e., expectoration of mucus, relief from fear of nightmares, etc.

The same factors which cause cardiac asthma by night may cause seizures during the day and result in more or less continuous dyspnea.

Four types of nocturnal dyspnea occur in patients with cardiac disease; these are orthopnea, evening dyspnea, Cheyne-Stokes respiration and cardiac asthma. They

all have a common underlying cause, namely, pulmonary congestion consequent to 'back pressure' from the left side of the heart.

Starr, Isaac, Jr.; Donal, J. S.; Margolies, A.; Shaw, R.; Collins, L. H.; and Gamble, C. J.: Studies of the Heart and Circulation in Disease; Estimations of Basal Cardiac Output, Metabolism, Heart Size and Blood Pressure in 235 Subjects. *J. Clin. Investigation* 13: 561, 1934.

Duplicate estimations of cardiac output together with determination of metabolism, blood pressure and pulse rate have been performed on 31 healthy persons and 204 hospital patients under conditions of basal metabolism. Orthodiagrams were secured also. The results have been subjected to statistical analysis.

The cases studied included patients with diseases not affecting the circulation, with hypertension, anemia, hyperthyroidism, neurocirculatory asthenia, valvular heart disease, various types of arrhythmia, coronary disease, acute endocarditis, and aneurysm; also patients who had recovered from congestive heart failure. Acute cardiac decompensation, advanced pulmonary disease, and the febrile diseases were not studied.

The condition of the circulation in the various forms of disease has been described and compared with the normal. The most unexpected finding was that the average basal circulation in cases of neurocirculatory asthenia was very abnormal.

Relationships by which the condition of the heart muscle might be ascertained have been sought for. Among normal persons and patients with normal hearts but abnormal circulation, the relationship between heart work per beat and heart size holds more closely than any other studied. In patients who have been once decompensated this relationship is abnormal almost without exception. It is believed, therefore, that it may be used to define normal myocardial function and to detect myocardial disease. Charts and equations are submitted by which the normality of any case can be decided.

Edwards, Joseph C., and White, Paul D.: A Note on the Incidence of Neurocirculatory Asthenia With and Without Organic Heart Disease. *New England J. Med.* 53: 211, 1934.

In an analysis of 5,000 consecutive patients with cardiac symptoms and signs seen in private practice in New England over a period of thirteen years, 687 patients (13.7 per cent) were found with definite neurocirculatory asthenia. Of the 687 cases, 448 (65.2 per cent) were uncomplicated by organic heart disease. One hundred and thirty-five (19.6 per cent) were complicated by organic heart disease, and there were 104 (15.2 per cent) in which neurocirculatory asthenia was present with doubt as to the presence or absence of organic heart changes. Of the 687 patients, 424 (61.7 per cent) were females and 263 (38.3 per cent) were males. Three hundred and fifty-four (51 per cent) of the 687 patients were in the age group from thirty-one to fifty years inclusive.

Of the types of organic heart disease found with neurocirculatory asthenia in our series, rheumatic heart disease was most frequent (44.4 per cent), coronary disease second (21.4 per cent), and hypertensive heart disease third (18 per cent). There was only one case of cardiovascular syphilis.

From this experience, the authors have found that the chances of a patient with symptoms of neurocirculatory asthenia coming to a consulting physician in New England to show no evidence of organic heart disease, are approximately three to one. Even though organic heart disease be present, symptoms may be entirely the result of a complicating neurocirculatory asthenia.

Book Review

L'INFARCTUS DU MYOCARDE. By Eduardo Coelho, Professor of the Faculty of Medicine and Physician to the Hospital of Santa Marta, Lisbon. Masson et Cie, Paris, 1934, 212 pages with 105 figures.

This monograph, published in French, consists of two parts: (1) an electrocardiographic study of experimentally produced myocardial infarction, and (2) a report of 28 clinical cases followed by a discussion of the etiology, clinical symptomatology, electrocardiography including localization, differential diagnosis and prognosis.

In the first part the author gives a satisfactory summary of his own important work on experimentally produced myocardial infarction and reviews the literature up to about two years ago. The advances since that time have been so great, however, that in certain important respects the discussion can scarcely be regarded as abreast of current knowledge.

The second part of the monograph, which deals with the clinical aspects of myocardial infarction, offers at most a minimal contribution. More than 60 pages are utilized for the protocols of the author's 28 cases and their electrocardiograms. The material is not remarkable. This part of the book is not up to the standards of several articles in English on the same subject.

C. C. W.

Errata

In the article by Dr. Max Winternitz, "The Initial Complex of the Electrocardiogram After Infarction of the Human Heart," published in the June issue (Vol. 9, p. 616) and translated from the German, a number of minor errors appear, of which the corrections are given below:

- P. 616, lines 29 and 30: We may find a deep Q_s apart from coronary thrombosis, with simple sclerosis without necrosis, and even as a variation of the normal electrocardiogram with certain rotations of the heart's axis.
- P. 618, line 14: . . . the widening of QRS, measuring 0.1 sec. . . .
line 17: . . . R_1 higher, just measuring 9 mm.
line 24: Dr. A. Ghon. . . .
- P. 620, line 7: . . . extensive myomalacia of the heart . . .
line 13: The duration of R_1 is unaltered but it has become smaller and splintered, . . .
line 18: Extensive old myomalacia. . . .
- P. 621, line 22: . . . he worked steadily, constantly suffering from stenocardia and epigastric pain.
- P. 622, line 28: . . . Siemens' oscillograph.
- P. 628, line 11: . . . cerebral, coronary and mesenteric vessels, . . .
- P. 629, lines 6 and 7: The initial complex shows slight notching in Leads I and III, small R in Leads II and III. . . .
- P. 630, line 12: . . . pain which lasted some hours. . . .
- P. 632, Legend to Fig. 14 . . . Siemens' oscillograph.
- P. 633, line 7: . . . strophanthin, 0.5 mg., . . .
- P. 633, line 27: QRS width 0.12 sec.
- P. 636, line 12: Cases of idioventricular rhythm . . .
- P. 641, line 18: . . . as is shown in their own illustrations.
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In the August issue in the article by Robb and Weiss: Page 762, second line, for 2.6 c.c. read 0.26 c.c.

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Original Communications

THE SELECTION OF CASES OF THROMBO-ANGIITIS OBLITERANS AND OTHER CIRCULATORY DISEASES OF THE EXTREMITIES FOR SYMPATHETIC GANGLIONECTOMY*

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THE application of sympathetic ganglionectionomy to selected types of disease of the peripheral arteries has marked a distinct advance in their treatment. Evaluation of this operation over a period of eight years has demonstrated conclusively a maintained and permanent vasodilatation of the peripheral arteries. In cases of spastic paraplegia, arthritis, and uncomplicated forms of Raynaud's disease, which are diseases without obliterative lesions in the arteries, vasodilatation is maintained at maximal levels as measured by thermometric and calorimetric methods.⁵ In diseases with occlusive lesions of the arteries of the extremities vasodilatation is maximal and permanent, provided the process of thrombosis is not progressive. The rationale of employing sympathetic ganglionectionomy in diseases with occlusive lesions is based on the demonstration of high degrees of vasoconstriction in the non-occluded major and collateral vessels. The diminished circulation in these diseases is the direct effect of two factors: (1) recurrent segmental occlusion of the arteries by thromboses, and (2) abnormal vasoconstriction in the nonoccluded arteries in the primary and collateral circulation. Vasoconstriction is measured indirectly by variations of the surface temperature of the acral areas. In occlusive arterial diseases the surface temperatures of the digits are usually low; that is, varying

*Read before the American Academy of Orthopedic Surgeons, Chicago, January 8, 1934.

From the Divisions of Medicine and Neurologic Surgery, the Mayo Clinic, Rochester, Minn.

between 22° and 27° C. As a result of a high environmental temperature, increases in the surface temperature are noted, but the range of fluctuation is restricted.

Recognition of the fact that both the obstructive and the vasomotor components contribute to the diminished circulation is important, as it provides an adequate explanation for the efficacy of sympathetic ganglionectomy in selected cases. Mulvihill and Harvey have shown that with ligation of the femoral arteries in the experimental animal the collateral circulation, as measured by the surface temperature, slowly returns to its preoperative level. If at the time of ligation the lumbar sympathetic ganglia are removed, recovery of the circulation is fairly complete within a period of twenty-four hours. The work of Baldes, Herriek, and Essex on dogs demonstrated that the flow of blood through the larger arteries, as measured by the Thermo-Stromuhr method of Reiss, was increased as much as 100 per cent on the side on which unilateral sympathetic ganglionectomy was performed.

The usefulness of sympathetic ganglionectomy in cases of occlusive diseases of the arteries has rested largely on the proper selection of those cases, and it was realized early that it would be futile to attempt to operate in all of them. In the older patients afflicted with arteriosclerosis obliterans the range of vasomotor activity is narrow, and the development of collateral circulation is less adequate (Horton) than in younger patients afflicted with thrombo-angiitis obliterans. Among these older patients also there is a greater operative mortality, as in many of them arteriosclerotic lesions of coronary, cerebral, and renal arteries are present.

THE VASOCONSTRICTION COMPONENT

Methods used.—Various methods have been employed to determine the amount of vasoconstriction present in the limbs. In 1926, one of us (Brown) described the use of nonspecific fever as a vasodilating agent. Fever is a most effective means of producing high degrees of vasodilatation. Foreign protein (Lederle's triple typhoid vaccine) is injected intravenously, and the temperature of the mouth and the surface temperatures of the digits of the extremities are measured every thirty minutes during the phase of fever. The procedure in detail, as we have carried it out at the Mayo Clinic, has been as follows: A room with constant temperature is used, with a range of environmental temperature controlled between 24° and 26° C. Thermocouples are applied to the various digits, and the readings are taken every ten minutes until a basal or constant level is obtained. Triple typhoid vaccine is injected intravenously in doses of 5 to 25 million killed organisms, depending on the size and sex of the patient. The following data are obtained: (1) the increase in the temperature of the mouth, (2) the increase in the surface temperature of the digits, and (3) the maximal vasodilatation level.

From these values three points are noted: (a) The vasomotor index (V. I.). (To determine this, the rise of surface temperature is divided by the rise in temperature of the mouth or blood, and the result represents the increase in surface temperature for each degree rise in the temperature of the mouth or blood. A vasomotor index of 2 or more is considered to indicate an abnormal degree of vasoconstriction.) (b) The vasomotor range (V. R.). (This is the rise in the surface temperature of the affected digits from basal to maximal levels with fever. A high degree of vasoconstriction is considered to be present if this increase is at least 4° C. or more.) (c) The maximal vasodilatation level (M. V. L.). (This is the highest temperature obtained in the affected digits. If it attains a level of 30° C. or more, a degree of vasodilatation adequate to justify operation is considered to be present in the affected digit.) In all the foregoing calculations the rise in the temperature of the mouth is deducted from the rise in surface temperature, so as to eliminate the actual increase in the temperature of the blood.

Morton and Scott have reported the use of general, local, and spinal anesthesia to obtain vasodilatation. These are satisfactory methods when the facilities are such that they can be employed as a routine procedure. Morton and Scott have postulated a "normal vasodilatation level" of 33° C., and the difference between this and the value obtained they have designated as the "obstruction index." White has employed injection anesthesia of peripheral nerves to prognosticate the effects of sympathectomy. Lewis and Collier and Maddock have used increased environmental heat, and Landis has suggested the immersion of both arms in water at 45° C. for a period of at least thirty minutes, which is followed by vasodilatation of the feet. We have studied the effects of various vasodilating drugs, including ethyl alcohol, given by mouth,⁸ acetylcholine,¹⁰ and theobromine,¹⁵ also those of hot drinks and increased environmental temperature. With all of them variable degrees of vasodilatation have been obtained. None of the procedures has produced the maximal dilatation responses comparable to those produced by fever or anesthesia.

SELECTION OF CASES OF THROMBO-ANGIITIS OBLITERANS FOR SYMPATHETIC GANGLIONECTOMY

Sympathetic ganglionectomy has had its widest application to thrombo-angiitis obliterans among diseases of the occlusive type. This disease is a chronic, inflammatory, obliterating arteritis, affecting chiefly the larger arteries of the arms and legs, and is characterized by a relapsing course. The thrombosis is inflammatory and is deposited in a segmental manner. The clinical aspect of the disease varies with the rapidity of the thrombosing process and the ability of the collateral circulation to keep pace. This point is important in attempting to interpret the effects of

treatment and in selecting cases for operation. In the majority of cases of thrombo-angiitis obliterans varying grades of vasoconstriction can be demonstrated. There is a close correlation between the severity and stage of the disease and the amount of vasoconstriction. In cases with a short history of claudication and marked diminution of the arterial blood supply to the digits there is marked rubor, diminished surface temperature and trophic changes in the skin, and the vasomotor component is usually low. Conversely, in cases with longer histories, two years or more, the signs of arterial insufficiency are not pronounced, the course of the disease is relatively slow, and the vasomotor component is relatively high.

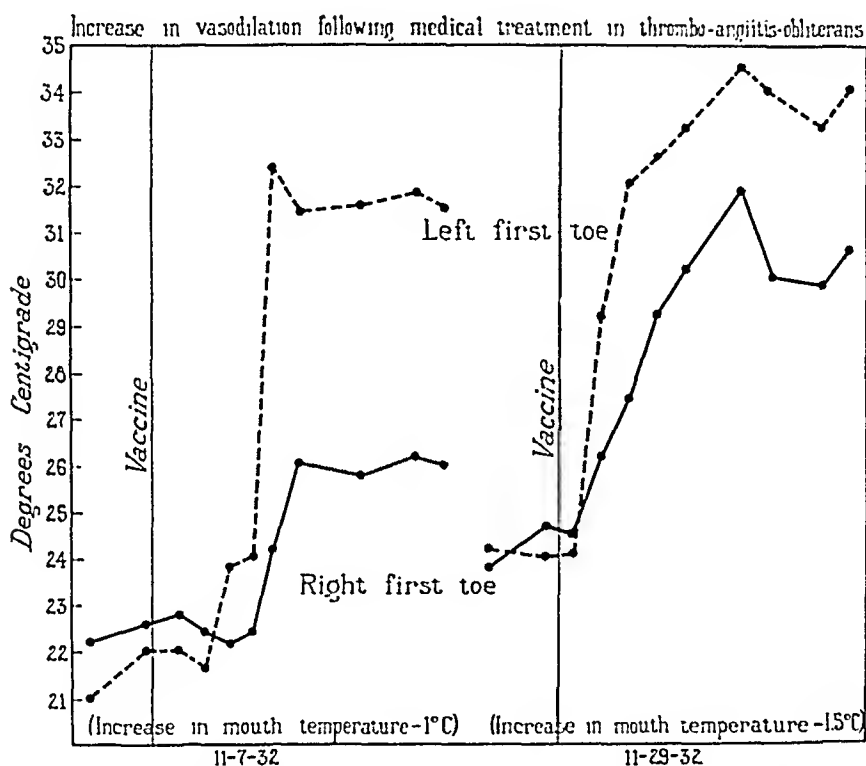


Fig. 1.—Increase in surface temperature with fever. The first determination shows incomplete vasodilatation in the first right toe. After a period of active medical treatment the vasodilatation in this digit showed a sharp increase sufficiently high to justify operation.

Selection of cases for sympathetic ganglionectomy rests upon two major points: (1) the demonstration of high degrees of vasoconstriction, and (2) the clinical aspects of the case. A mathematical expression as a basis for instituting operative measures constitutes only one determinate, and it should not exclude the obvious clinical features that are of equal importance. These are: (1) The general condition of the patient. Many patients who have suffered greatly from pain, loss of sleep, or from excessive use of tobacco or opiates, should not be subjected to a major operation without a preoperative period of treatment.

Coronary disease is not an uncommon complication of thrombo-angiitis obliterans, and sudden death in this disease does occur. (2) The occupational hazards with respect to the extremities, if the livelihood of the patient depends on the use of the feet or hands, or if his occupation involves exposure to the rigors of the weather in northern climates, the need of the operation for protection is clear. (3) The stage of the disease. We are of the opinion that certain failures of this operation to obtain the expected results have been due largely to the fact that it has been carried out during a stage of acute advanced arterial insufficiency in the presence of ulcers and severe rest pain. We have amply demonstrated that sympathetic ganglionectomy is not effective in this phase of the disease. Before operation is undertaken, it is extremely important to control the pain by adequate medical treatment and to demonstrate the potentiality of the ulcer for healing. A period of active treatment and a lapse of time will frequently demonstrate a sharp increase in the vasomotor component (Fig. 1). A low vasomotor component is usually found in digits with ulcers or trophic lesions, or during the period of acute arterial insufficiency following recent thrombosis. If fever therapy and other medical measures do not relieve the pain, initiate healing, and demarcate the gangrenous tissues, it has been our experience that operative measures are likely to fail.

THROMBO-ANGIITIS OBLITERANS WITH LUMBAR GANGLIONECTOMY

To determine the validity of prediction based on preoperative studies of the vasomotor components, the vasomotor indices, the vasomotor range, and maximal vasodilatation level have been compared with the postoperative surface temperatures in the same digits, taken at varying intervals after operation. Complete data are here presented from fifty-five cases of thrombo-angiitis obliterans in which lumbar sympathetic ganglionectomy was performed and in which temperature studies were complete (Table I). The average vasomotor index for the group was 4.4. In this group were eleven cases in which vasomotor indices were below 2. Operation was carried out because of the relatively high values obtained for the other vasomotor factors and the favorable clinical aspects of the cases. The number of cases with low indices was insufficient to make a correlation with the postoperative increases in the surface temperature. In the group with vasomotor indices less than 2, the maximal vasodilatation level attained by operation was approximately 2° less than in the group with vasomotor indices more than 2. In the majority of cases the operation was carried out only when vasomotor indices were relatively high.

Vasomotor range.—Increase in temperature with fever was 5.6° C. compared with increase from operation of 5.4° C., a remarkably close

TABLE I
COMPARATIVE EFFECTS OF FEVER AND SYMPATHETIC GANGLIONECTOMY:
AVERAGE VALUES

	MAXIMAL TEMPERATURE, DEGREES C.		INCREASE* IN TEMPERATURE		VASO- MOTOR INDEX
	WITH FEVER	AFTER OPERATION	WITH FEVER	AFTER OPERATION	
Thrombo-angiitis obliterans					
Toes	31.5	31.3	5.6	5.4	4.4
Fingers	32.7	30.8	6.7	4.8	4.7
Raynaud's disease					
Toes	32.3	33.7	8.0	9.4	6.9
Fingers	34.4	31.1	9.2	5.9	7.8
Scleroderma					
Toes	33.7	30.9	9.3	6.5	7.8
Fingers	34.6	31.3	8.6	5.3	6.5
Arthritis					
Toes	33.2	32.7	7.1	6.6	4.6
Fingers	35.7	33.4	8.7	6.4	4.5

*Mouth temperature deducted from these values.

approximation. The average maximal vasodilatation level obtained with fever was 31.5° C. as compared with 31.3° C. obtained with operation.

THROMBO-ANGITIS OBLITERANS WITH CERVICODORSAL GANGLIONECTOMY

There were twelve patients in this group, all of whom had trophic lesions involving the fingers. The bilateral operation was done in all cases. The average vasomotor index for the group was 4.7, and in no case was it lower than 2.2. There was no close correlation between the vasomotor index and the postoperative surface temperatures. The vasomotor range of the fingers with fever showed a mean increase of 6.7° C. as compared to 4.8° C. increase with operation. The maximal level of vasodilatation for the group with fever was 32.7° C. as compared to 30.8° C. obtained with operation.

In the upper and lower extremities there are significant differences in the response of the surface temperature with fever and with sympathetic ganglionectomy. In the feet the approximations in the surface temperature are extremely close with fever and with operation, for the vasomotor range and maximal vasodilatation. In 90 per cent of the cases the variation was less than 1.5°. When greater variation was obtained, a technical error may have been accountable, or thrombosis may have occurred in the interval. In the hands the vasodilatation from fever exceeded by significant differences that obtained by operation. This may be explained in part by the fact that in some of our early cases in which operation had been performed there occurred incomplete removal of the vasomotor fibers, as determined by sweating tests. A further explanation is that after sympathetic denervation there is some

fundamental difference in the behavior of the autotonus of the arteries of the hands as compared to that in the feet. It was observed that in cases in which complete sympathectomy had been performed the variation in the surface temperature of the fingers to environmental changes was greater than that in the toes after lumbar sympathectomy.

RAYNAUD'S DISEASE WITH LUMBAR SYMPATHETIC GANGLIONECTOMY

There were nine cases in this group. The average values for vasomotor indices, vasomotor range, and maximal vasodilatation levels are shown (Table I). The vasomotor indices were high in all but one instance; the

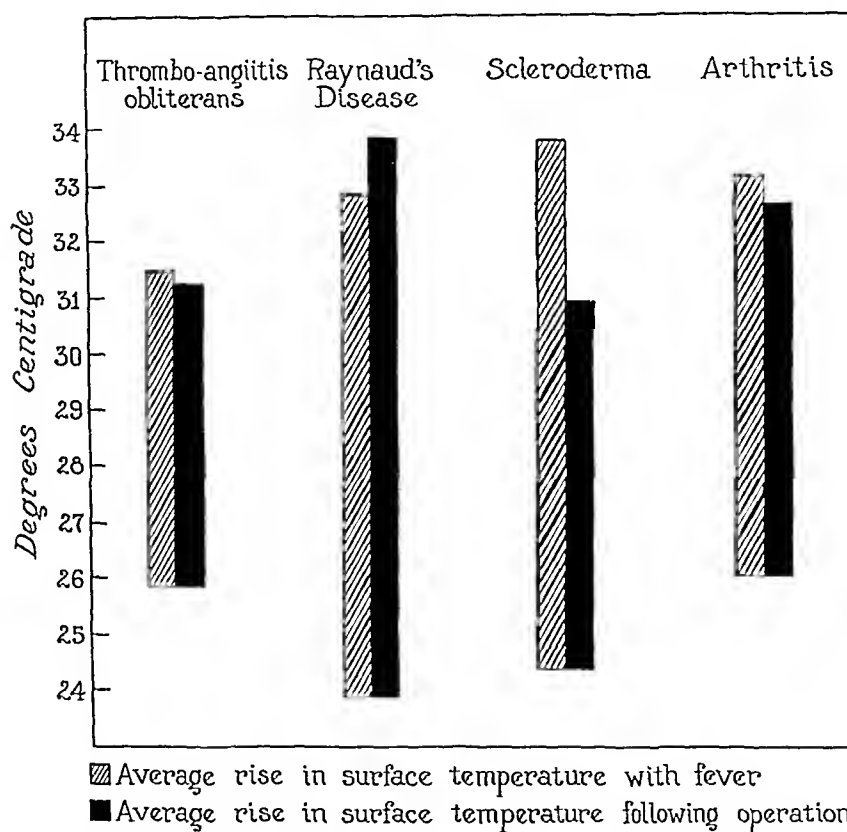


Fig. 2.—The effect of fever and lumbar sympathectomy on surface temperature.

average was 6.9. The vasomotor range with fever was 8° C. as compared to 9.4° C. with operation. The maximal level obtained with fever for the group was 32.3° C., as compared to 33.7° C. with operation. In two cases much higher values were obtained after operation than were obtained with fever (Fig. 2).

RAYNAUD'S DISEASE WITH CERVICODORSAL SYMPATHETIC GANGLIONECTOMY

There were thirteen cases in this group. Vasomotor indices were high in all cases, averaging 7.8; in none were values lower than 4 noted. The vasomotor range was 9.2° C. with fever and 5.9° C. increase in surface

temperature with operation. The maximal vasodilatation level was high with fever averaging 34.4°C ., as compared to 31.1°C . with operation (Fig. 3).

In Raynaud's disease the correlation of the preoperative and post-operative surface temperatures with fever is not so close as in thrombo-angiitis obliterans. If the diagnosis is correct and trophic lesions are slight, high grades of vasodilatation will be obtained with fever and with complete sympathectomy. The usefulness of preoperative studies of the vasomotor component is distinctly less than in thrombo-angiitis obliterans. It is interesting to observe that as in thrombo-angiitis oblit-

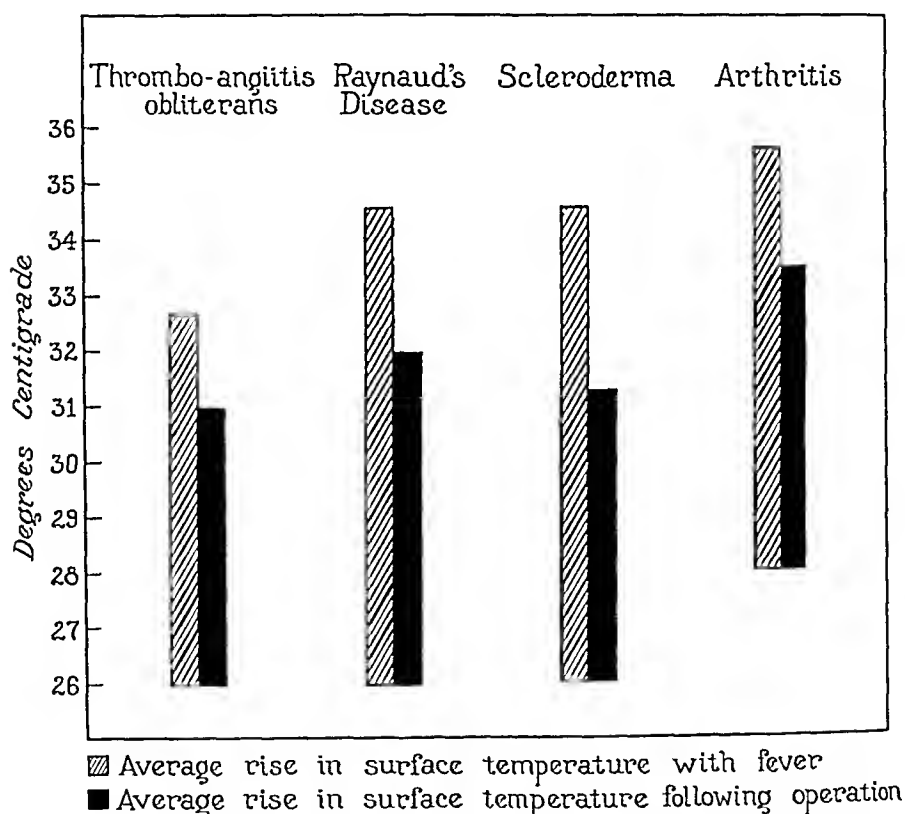


Fig. 3.—The effect of fever and cervicodorsal sympathectomy on surface temperature.

erans, higher grades of vasodilatation occurred in the hands with fever than in the toes. Vasodilatation from operation in the hands was significantly less than that with fever, whereas in the feet higher grades of vasodilatation followed operation than were obtained with fever.

SCLERODERMA

There were twenty-four cases in this group (Table I). Cervicodorsal ganglionectomy was performed in fifteen and lumbar ganglionectomy in eight. Vasomotor indices were high in the entire group. The average value for the fingers was 6.5, and for the feet, 7.8. No close correlation between these indices and the postoperative surface temperatures was

found. The vasomotor range had a greater increase with fever than with operation, and a similar discrepancy was demonstrated in the comparison of the maximal vasodilatation levels. The average high point in the same digits was 34.6° C. with fever and 31.3° C. with operation. In the group of nine cases in which lumbar ganglionectomy was performed the average vasomotor range with fever was 9.3° C. and with operation 6.5° C. The maximal vasodilating level with fever was 33.7° C. and with operation 30.9° C.

The greatest discrepancy between the vasodilatation with fever and that with operation was shown in cases of scleroderma with vasomotor phenomena. This held true for both feet and hands. Incomplete operation would not explain this difference in the feet, as incomplete sympathectomy has not occurred in lumbar ganglionectomy. There are pathological changes in the skin and subdermal structures in scleroderma which do not exist in other vascular diseases.² There is a quantitative diminution in the capillaries, and obliterative lesions are demonstrable in the digital arteries. The increased density of the cutaneous tissues may increase radiation of heat during fever producing abnormally high surface temperatures, and they are not solely a result of dilatation of cutaneous arterioles. The problem of selection of cases of scleroderma for sympathetic ganglionectomy is difficult, and the results of operation have not been comparable to those obtained in the other forms of circulatory diseases without dermal involvement. Slightly higher grades of vasodilatation from operation were noted in the hands than in the feet.

ARTHRITIS

In this group there were five cases in which cervicodorsal ganglionectomy was done. The vasomotor indices and vasomotor range were high in the hands, averaging 4.5° and 8.7° C., respectively; the postoperative surface temperatures were high in all cases. The maximal surface temperatures were 35.7° C. with fever and 33.4° C. with operation.

In all of the thirteen cases in which lumbar sympathectomy was performed the vasomotor indices, ranges, and maximal surface temperatures were high with fever, and postoperative surface temperatures averaged 32.7° C. For the group there was 0.5° C. greater increase with fever than with operation (Table I).

In arthritis, sympathectomy was carried out in the presence of abnormal degrees of vasoconstriction and localization of the arthritis in the peripheral parts. No organic lesion of the arteries was present, and the maximal grades of vasodilatation were obtained with fever and with operation. In the group a higher grade of dilatation from operation was obtained in the hands than in the feet, which is contrary to the

effect observed in thrombo-angiitis obliterans and in Raynaud's disease. Removal of the lumbar and cervicodorsal ganglia in patients with arthritis demonstrated conclusively the effectiveness and permanency of vasodilatation. Many of these cases have been followed and surface temperatures tested repeatedly over a period of years. In none have the surface temperatures shown values less than 30.7° C. in the hands and 31.8° C. in the feet. Preoperative studies of the vasomotor components did not give important prognostic information in the cases of arthritis.

COMMENT

Prediction of the degree of vasodilatation that may be expected from sympathetic ganglionectomy is possible within certain limits. The limitations are related to the character of the disease, the completeness of operation, and the presence or absence of abnormal changes in the skin, such as infections, ulcers, and fibrosis. In purely vasospastic disturbances vasodilatation will take place if the operation is complete, and preoperative procedures are not necessary for prognosis. Arthritis and early cases of Raynaud's disease fall in this group. In the presence of occlusive disease of the arteries determination of the available vasodilatation is important. Vasomotor control of the collateral vessels has been well shown in the experimental animal. Mulvihill and Harvey have demonstrated a rapid restoration of the peripheral circulation when sympathetic ganglionectomy was done after the iliac arteries were ligated. In man, after sympathetic ganglionectomy, the increase in circulation is variable in the presence of occlusive disease of the peripheral arteries. Several factors are responsible for this: first, the collateral circulation may be involved in the occlusive disease; second, collateral circulation may be incompletely developed because of the rapid progress of the obliterating process, and third, the presence of ulcers or gangrene impairs vasodilatation in the area thus affected. The demonstration of high grades of vasodilatation before operation does not give accurate prognostic information as to the subsequent course of the occlusive disease, and this fact needs emphasis in respect to thrombo-angiitis obliterans. For prognosis the clinical course is as important as the available vasodilatation in a given stage of the disease. This operation is a therapeutic procedure of high efficacy in that the maximal available vasodilatation will be obtained, but it will be modified by the subsequent course of the obliterating disease. The problem in a given case is whether this maximal vasodilatation will relieve pain, effect healing of an ulcer, or modify relapsing thromboses. In the absence of ulcers or pain the operation is advocated for its protective function by preventing or minimizing subsequent trophic lesions. This protective function has been

amply demonstrated. In cases of ulcers, edema, and rest pain, evidence of healing and pain relief should be demonstrated by medical measures before operation is advised.

The demonstration of an abnormal degree of vasoconstriction in the extremities by fever or anesthesia is one of the requisites for advising operation in thrombo-angiitis obliterans. Fever produces effective dilatation in 98 per cent of the cases. Two of our patients failed to obtain dilatation with anesthesia but showed vasodilatation with fever. The problem in the selection is, what values or limits of vasodilatation should be established to make operation advisable? In our early work with the vasomotor index it was felt that the surface circulation should show an increase at least twice the rise of temperature in the mouth or blood. This divided the cases into two groups, those with excessive and those with minimal degrees of vasoconstriction. From the clinical standpoint this was satisfactory, and the results demonstrated the usefulness of this criterion. Later the rise in surface temperature (vasomotor range) was studied, and an increase of at least 4° C. was established as an index for operation. Certain errors could develop in both of these methods, in that a basal surface temperature could not always be obtained, and during hot weather the surface temperature could be high, thus giving abnormally low values. The maximal surface temperature of the digit most affected was then taken as a basis for prediction. This could not be affected by shifts in the surface and environmental temperatures. Preoperative and postoperative studies showed that this value gave the highest correlation and was less subject to error. A maximal surface temperature of 29° C. or higher with fever was regarded as necessary for justifying operation.

It must be kept in mind that thrombo-angiitis obliterans is a relapsing disease. There is no conclusive proof that ganglionectomy prevents recurrence of thrombosis. We believe it decreases the incidence of recurrence, but we have seen several patients in whom recurrences of arterial thrombosis have taken place months after operation. The protective nature of the operation against loss of limbs was demonstrated in these cases.

The selection of cases for sympathetic ganglionectomy in other types of vascular disease by quantification of the vasomotor component is not crucial. In cases of Raynaud's disease a high degree of vasoconstriction is the rule. Superficial ulcers, secondary infections, and thrombosis of the digits may produce variations in different digits.

In vasomotor forms of scleroderma affecting the extremities vasomotor studies are of some value. However, it has been our experience that the postoperative temperatures do not attain the levels of surface temperatures resulting from fever. Injections of opaque substances into the arteries in cases of scleroderma have shown that in this disease

there are occlusive lesions of the smaller arteries or arterioles.³ Further, there is a quantitative diminution of the capillaries in the skin, and also secondary changes in the subcutaneous tissues which are irreversible and which cannot be restored by operation. There is, however, a certain protective value against the progression of the disease and the subsequent development of ulcers and progressive fibrosis.

In arteriosclerosis obliterans we do not believe that sympathetic ganglionectomy is advisable. There may be an occasional case in which patients are in the fifth or sixth decade of life where it can be used with beneficial results. Most of these patients, however, have other foci of arteriosclerosis, and in these the risk is abnormally high. It is unwise to employ the use of fever in arteriosclerotic subjects, because thrombosis tends to develop in these patients.

SUMMARY

Sixty-seven cases of thrombo-angiitis obliterans have been studied to determine the prognostic value and relation of the peripheral vasodilatation attained with systemic fever to the increase of surface temperature following sympathetic ganglionectomy. A close approximation is shown. This correlation is higher in the feet than in the hands. Other factors in the selection of cases of this form of vascular disease for operation are important, particularly those of the integrity of the coronary arteries, the rate of progression and stage of the disease, and the ability to demonstrate healing and relief of pain by medical measures. About one-third of the cases are suitable for operation. Pre-operative determinations of the vasomotor component are less essential in the pure vasomotor disorders and in arthritis. Maximal grades of vasodilatation will result if the operation is complete.

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THE POSITION OF THE HEART VALVES AND THEIR RELATION TO THE ANTERIOR CHEST WALL IN LIVING SUBJECTS WITH ABNORMAL HEARTS*

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THE position of the heart valves in relation to the chest wall is of great significance in physical diagnosis. However, surprisingly little is known about it, particularly when the heart is enlarged. The method of dissection in the hands of anatomists has concerned itself chiefly with hearts of normal size, and even here there is considerable difference in the descriptions given by different anatomists. Methods used by them to localize the valves could hardly be termed satisfactory, and distortion from the position in life easily was possible. Roentgen ray methods seem to have been applied in only three studies, those of Groedel (1912),¹ of Norris and Fetterolf (1912 and 1913)^{2, 3} and of LeWald (1916).⁴ Groedel studied hearts removed from the chest and so threw no light on the relation of the valves to the chest wall. Norris and Fetterolf cut the thorax of 15 cadavers, preserved by formalin and frozen, into frontal sections one inch thick parallel with the anterior chest wall, separated the sections and covered the surfaces of the heart valves with lead paint; after superimposing these sections in order, roentgenograms were taken, and the shadows of the valves, covered with lead paint, appeared in their true position in the roentgenograms. LeWald followed the general plan of Norris and Fetterolf but localized the valves by inserting metal rings from the auricular side into the position where the valves joined the heart wall. Roentgenograms were taken in the postero-anterior, lateral and superior planes; these revealed unequivocally the position of the valves in the one cadaver studied. All of these studies showed the valves as located close together; the methods used did not exclude changes in position that might easily have occurred following death, and were of no help in localizing the valves in abnormal hearts. Physical examination of patients with abnormal hearts and especially those that were greatly enlarged has thrown doubt on the fixed relationships of heart valves to chest wall, as indicated by these anatomical studies.

Our observations on the visualizing in the living patient of calcium deposits in the aortic and mitral valves and in the annulus fibrosis of the mitral valve have given us a method of localizing the position of the

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heart valves in relation to the chest wall. These show that the actual position of the valves in the living subject varies greatly from patient to patient.

Technic.—The roentgenological and fluoroscopic technic has been discussed in detail in our previous report.⁵ To locate these calcified valves fluoroscopically, adequate preparation of the eyes is essential. A four-and-one-half- to five-inch gap (70-75 K.V. self-rectified) with five milliamperes of current usually is sufficient. A very small aperture should be used to eliminate secondary radiation. Observing these precautions the auriculoventricular junction on the left border of the heart con-

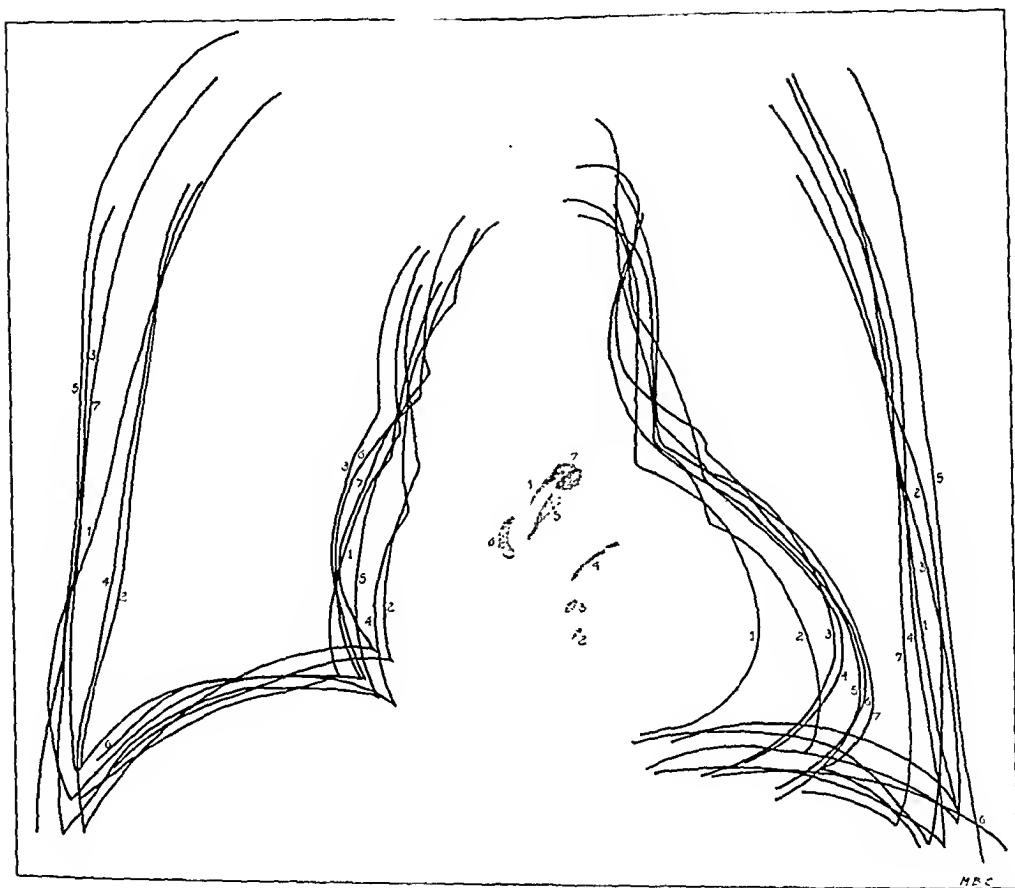


Fig. 1.—Seven superimposed orthodiagrams of aortic stenosis with calcification. The calcified deposit, left and right cardiac borders, and chest walls have been similarly numbered in each case.

tour may be located by its V-shaped depression and lack of pulsation. A search through the heart shadow below and medial to this point will disclose the dancing shadows cast by the calcium deposits if they are present in the mitral area. Calcifications in the aortic area usually are hidden by the vertebral column in the postero-anterior projection making oblique positions indispensable. A slight right antero-oblique position is best for visualization of the calcified aortic valves. Deep inspiration with an arrest of the respiratory cycle often helps in differentiating shadows in the lungs and mediastinum from those in the heart.

For radiograms it was found satisfactory to use an exposure of one-thirtieth of a second with a maximum milliamperage of 200, distance of thirty inches, using

fast screens and speed films, and a two-and-one-half-inch cylinder, directed accurately at the valve, to cut down secondary radiation.

The orthodiagrams were prepared in the usual manner. A skin pencil with a lead sheath (making it visible through the fluoroscope) was used to trace out the cardiac outline and valve positions on the patient's chest using at all times a small aperture and parallel rays. The ribs were sketched in afterward and photographs taken in the standing position. For diagrammatic and demonstration purposes these outlines were also traced on clear roentgen films.

As a result of these studies we present two diagrams showing the position of the calcified portions of the aortic and mitral valves. Fig. 1

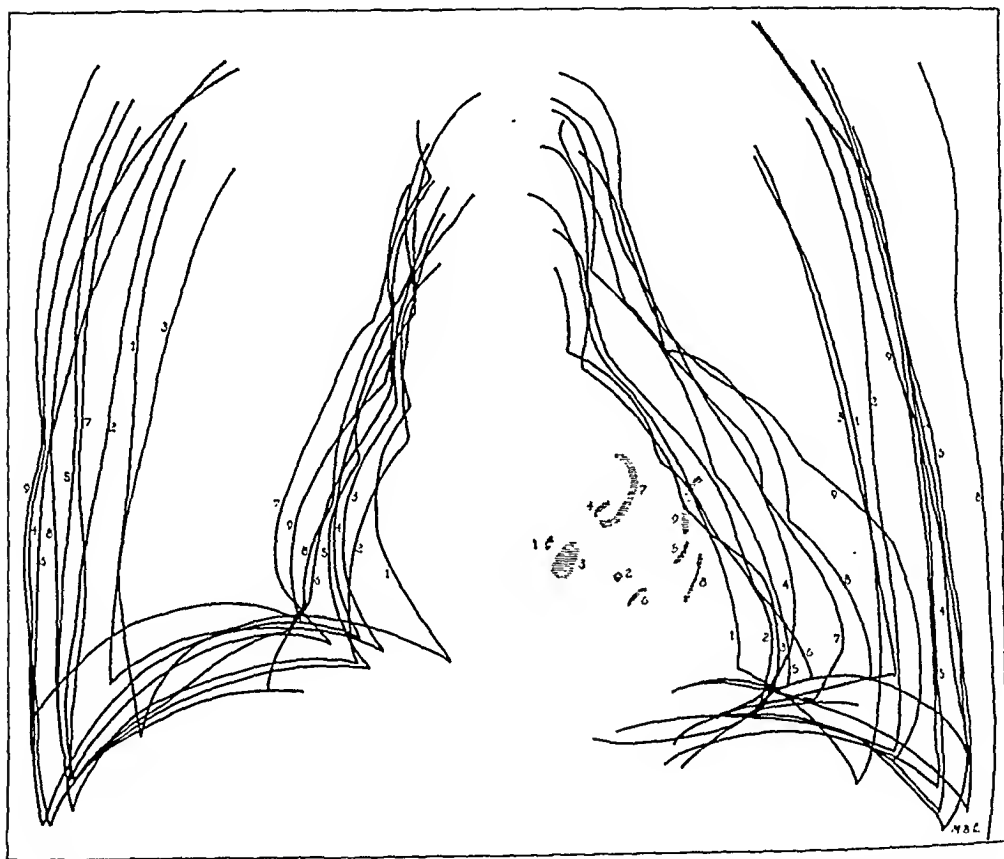


Fig. 2.—Nine superimposed orthodiagrams of mitral stenosis with calcification. The calcified deposit, left and right cardiac borders, and chest walls have been similarly numbered in each case.

shows superimposed orthodiagrams of seven cases of aortic stenosis with calcification; it shows the outline of the heart borders and the chest wall numbered the same as is the corresponding calcified area for that particular heart. The variation in the location of the valves is easily seen.

Fig. 2 represents nine superimposed orthodiagrams of mitral valve calcifications similarly numbered. Fig. 3 represents orthodiagrams of six cases of calcifications in the annulus fibrosis also similarly numbered. These show the larger semicircular calcified areas which partially sur-

round the mitral valve and anatomically form the attachment for the valve cusps. Also in these hearts of older patients the degree of enlargement is seen to be less.

Fig. 4 shows two cases of aortic valve calcification. The variability of the valve position in relation to the xiphoid process is clearly brought out. In Case B the mark for the valve calcification is seen to be immediately over the xiphoid process. This patient was proved to have aortic valve calcification by post-mortem examination. There is no way to reconcile this low position of the valve with the textbook position

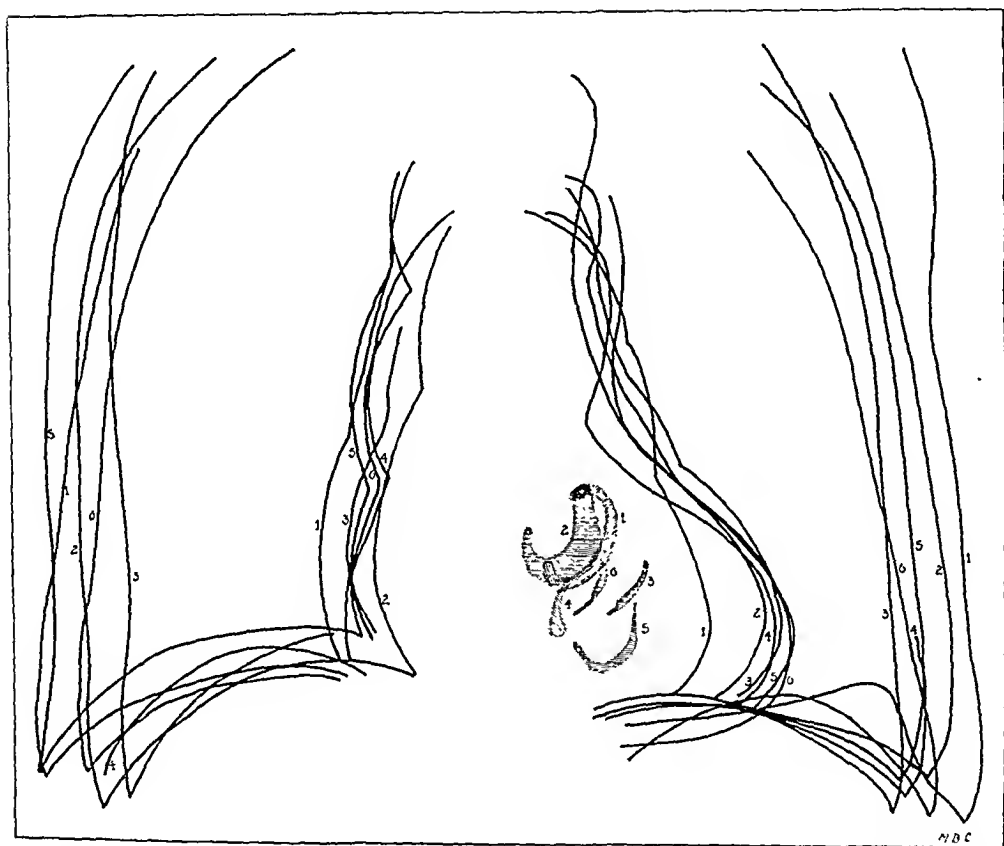


Fig. 3.—Six superimposed orthodiagrams of mitral annulus fibrosis calcification. The calcified deposit, left and right borders, and chest walls have been similarly numbered in each case.

unless we consider the explanation to be an elongation of the aorta with consequent depression of the right border downward and a rotation of the apex outward.

Fig. 5 shows two cases of calcified mitral valves. Noting the great difference between the heart contours of these two patients one would not expect the valve positions to be similar. The left auricular hypertrophy in Case D is posterior. The calcification in the mitral valve has been confirmed by pathological examination.

From these observations the following deductions may be drawn with regard to the position of the aortic and mitral valves in patients with abnormal hearts:

1. Both valves are likely to be found on a line 45 degrees from the horizontal, starting at the auriculoventricular groove on the left border

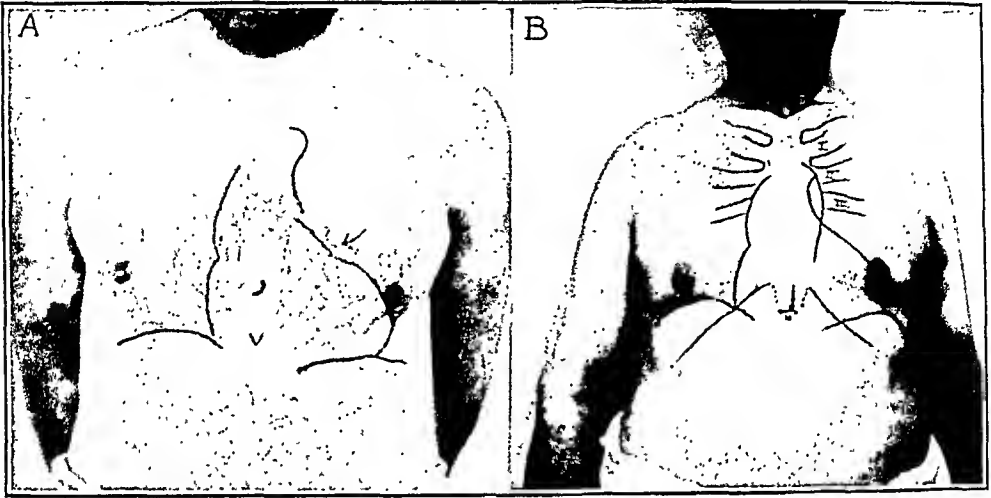


Fig. 4.—Two cases of aortic stenosis with calcification. The curved line near the midline represents the position of the calcified valve in Case A. The xiphoid process is shown by "v." The arrow on the left border marks the auriculoventricular junction. In Case B the calcified valve is seen to be directly over the xiphoid process.

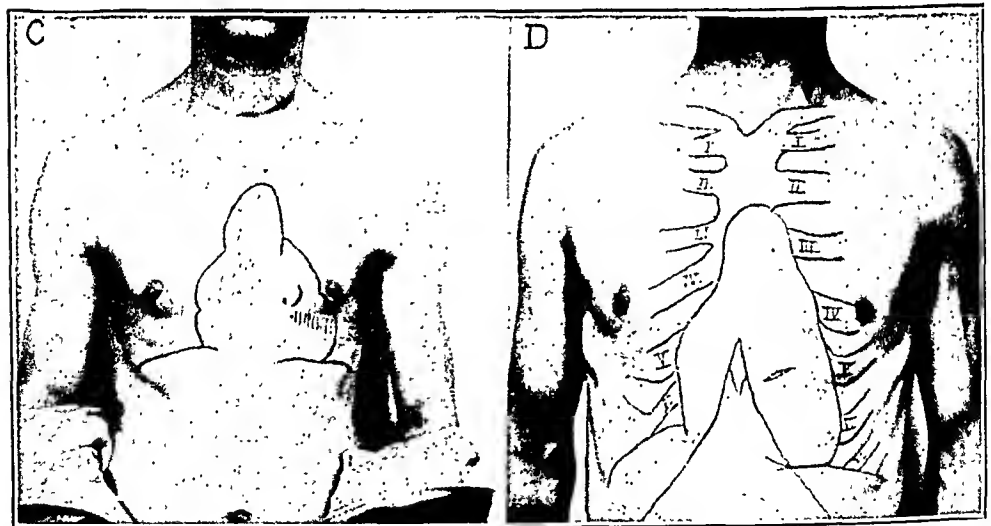


Fig. 5.—Two cases of mitral stenosis with calcification. The vertical lines below the calcified area in Case C represent the area where the thrill was of greatest intensity. Case D shows the calcified area to the left of the xiphoid process. The auricular bulge in Case D was most marked posteriorly.

of the heart shadow, this line corresponding to the position of the auriculoventricular groove. Fluoroscopically the calcified aortic valve if not on this line is likely to be medial to or above it, while the mitral valve varies lateral to and below it.

2. The mitral valve is likely to be more to the left of the midline than the aortic valve, and the latter may be exactly in the midline.

3. The aortic valve usually is more caudad than the mitral valve in relation to the chest wall, but may be more cephalad in relation to the total bulk of the heart shadow. This is probably due to the predominance of the left ventricle in aortic disease and to the large dilated auricles in mitral disease.

4. In the right anterior-oblique position the two valves may occupy the same position in relation to the cardiac outline, so that this view, although the one in which it is easiest to see the valves, is of no value in determining which valve is calcified.

5. The left anterior-oblique view is the best for differentiating between aortic and mitral valve calcifications, but is the most difficult, because in this position the roentgen rays must traverse the maximum thickness of the heart. Small areas of calcifications visible in the other oblique view may not be visible in this view. If large enough to be seen in the left anterior-oblique position, the mitral valve calcifications will be found to lie in the posterior one-third of the heart shadow, while the aortic valve calcifications are usually in the middle one-third. If the posterior cusp of the mitral valve is calcified, it may be within one centimeter from the posterior surface of the heart shadow. The chief difficulty lies in deciding between calcification of the anterior mitral leaflet and that of the posterior aortic cusp. (It is important in this position to have the posterior surface of the apical portion of the heart just clear of the shadow of the spine.)

6. In calcified annulus fibrosis cases the shadows are likely to be larger and denser, usually J-, O- or U-shaped, and on the films are more homogeneous in appearance than the irregularly mottled calcifications in the mitral leaflets. They occur frequently in patients without discoverable heart disease (although several cases of calcified mitral annulus fibrosis had slight aortic stenosis, uncalcified) and are usually found in patients sixty years of age or older.

7. If both valves are calcified, they may move independently; i.e., their dancing excursions with the heartbeat are not synchronous, but are consecutive. Further details on this part of the problem await the development of an accurate timing mechanism.

CONCLUSION

Great variations in position of the aortic and mitral valves occur as the heart enlarges or otherwise changes its relations to the thoracic cavity. This has an important bearing on the localization and distribution of murmurs and is of great significance in the interpretation of physical signs.

The authors wish to express their sincere appreciation to Dr. Henry A. Christian for his many helpful suggestions and valuable criticisms.

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THE INTERPRETATION OF THE GALVANOMETRIC CURVES OBTAINED WHEN ONE ELECTRODE IS DISTANT FROM THE HEART AND THE OTHER NEAR OR IN CONTACT WITH THE VENTRICULAR SURFACE*

PART I. OBSERVATIONS ON THE COLD-BLOODED HEART

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INTRODUCTION

IN A RECENT study of the electrocardiographic changes that follow the ligation of a large coronary artery we made extensive use of leads in which one electrode was placed very near the heart or in contact with its exposed surface and the other as far from the heart as possible. In the course of this study the correct interpretation of the curves so obtained became a matter of importance, and certain questions that arose in this connection led us to investigate the following subjects: (1) The changes that curves obtained by leading directly from the exposed heart, in the manner described, undergo when the heart is completely immersed in a conducting medium and the direct contact is moved away from its surface. (2) The nature of the electrical responses of injured heart muscle and the factors that influence their form in direct and semidirect leads. (3) The potential variations that occur in the ventricular cavities and the relations between them and the potential variations recorded at the epicardial surface. Part I of this paper deals with experiments performed on turtles. In these experiments only the first two of these subjects were studied. Part II (published separately) deals with a series of observations on the mammalian heart, concerned, for the most part, with the third subject listed.

In studying the first of these problems we had in mind the objections raised by Bishop and Gilson¹ to the interpretation placed by Craib² on certain curves which he obtained by leading directly from the air-exposed surface of tissues partly immersed in a conducting medium. A few words of explanation are perhaps desirable. It can scarcely be doubted that the electric currents produced by an excitable tissue completely immersed in an extensive conducting medium are distributed in accordance with the laws that define the flow of electric currents in volume

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conductors. From the character of these laws it follows that a curve obtained by pairing an electrode very close to the tissue with an electrode very far from it may be regarded as representing the potential variations of the former (Wilson, Macleod and Barker³). By comparison the potential of the distant electrode must be very nearly constant. Craib² employed such leads in studying the action currents of immersed and partly immersed tissues and interpreted his records in accordance with this principle. He made no distinction, and apparently saw no difference, between those experiments in which the tissue and the near electrode were fully immersed in the conducting medium and those in which the tissue surface with which this electrode was in contact was exposed to the air. He evidently regarded the tissue itself and the film of fluid adhering to its air-exposed surface as merely a part of the surrounding conductor. With this opinion we are in complete agreement. Bishop and Gilson adopted a different point of view, and criticized Craib's conclusions on several grounds. In their paper they ignored the laws that define current flow in volume conductors, and treated experiments of the kind mentioned as if the various conductors involved were parts of a network. They attributed many of Craib's findings to asymmetry of the tissue environment. According to their view it is not legitimate to assume that the potential variations of the distant electrode are negligible when this electrode is paired with an electrode in contact with the air-exposed surface of a partly immersed tissue. They spoke of the direct contact, when so placed, as partially insulated from the surrounding medium, and implied that its potential variations are entirely different from those that would occur in the medium near the point with which it is in contact if the tissue were completely submerged.

If these conclusions are correct and apply to leads from the exposed heart, it is not permissible to interpret the ventricular complexes obtained by precordial and by semidirect leads in accordance with the principles that apply to the interpretation of curves obtained by leading directly from the ventricular surface. Although our previous experience led us to believe that semidirect leads from a given region on the surface of the immersed heart and direct leads from the same region when it is exposed to the air yield curves of strikingly similar outline, it seemed desirable to obtain further information on this point.

In studying the responses of injured heart muscle we had several objects in view. We sought, first of all, to arrive at a more complete understanding of the factors that determine the direction and magnitude of the displacement of the RS-T segment of the ventricular complex which occurs immediately after the ligation of a coronary artery. As has frequently been observed, the same phenomenon is seen whenever the heart muscle is injured locally. In the second place we desired to con-

firm and extend the observations made by Wilson, Macleod and Barker³ and to test the utility of the hypothesis advanced by them to explain the monophasic responses obtained from injured tissues partly or completely immersed in a conducting medium.

METHODS

Our first experiments were carried out on turtles (*Graptemys geographica*). The animal was pithed, and the heart was exposed by removing the plastron or by cutting out that portion overlying the heart with a trephine. Two string galvanometers arranged in tandem enabled us to obtain two simultaneous records on the same film. One of these galvanometers was used in the ordinary way; the other was connected to the balanced plate circuit of a vacuum tube operating at its free grid potential (Wilson, Johnston, Macleod and Barker⁴). One terminal of each apparatus was attached to an Ag-AgCl electrode placed as far as possible from the heart. In some instances these indifferent electrodes were placed on the tail or one of the hind legs. In other instances the turtle was placed on its back in a large shallow dish filled with Ringer's solution with which the indifferent electrodes were in contact at a point as far from the animal as possible. The other terminal of each apparatus was attached to an exploring electrode which could be placed on or near the heart as desired. The exploring electrodes consisted of small glass tubes stoppered with salted kaolin and filled with Ringer's solution into which a coil of silver wire coated with silver chloride was thrust. The contact with the heart was made by a wick imbedded in the kaolin plug and allowed to project several millimeters beyond the glass tube. In some instances this wick was left bare; in others it was inclosed in a small rubber tube so that it was insulated to within one or two millimeters of its end. When such electrodes are placed in a conducting medium, the effective electrode surface is, of course, at the end of the insulated shaft.

DESCRIPTION OF EXPERIMENTS

In describing illustrative experiments it will be convenient to differentiate between the two exploring electrodes by calling one of them the x-electrode and the other the y-electrode. We shall use the former term to designate the electrode connected to the galvanometer responsible for the upper curve in our records, and the latter to designate the electrode connected to the grid terminal of the vacuum tube amplifier and thus indirectly to the galvanometer responsible for the lower curve. The connections were always so made that relative negativity of the exploring electrode produced an upward deflection. The time intervals shown on the records are fifths of a second.

Experiment I. The heart was exposed by trephining the plastron, and the animal was placed in a shallow dish containing Ringer's solution. The indifferent electrodes were in contact with this solution at a point 16 cm. from the nearest part of the turtle. The wick of the x-electrode was bare and extended 3 mm. beyond the glass shaft. The wick of the y-electrode was inclosed in a small rubber tube which extended to its tip. Both exploring electrodes were placed in contact with the ventricle approximately at the center of its ventral surface. They were very close together. After taking control curves (Fig. 1 *A*) the heart was flooded with saline (0.9 per cent NaCl) to a depth of approximately 8 mm. This resulted in a conspicuous reduction in the size of both curves (Fig. 1 *B*), but the upper curve fell off more in proportion to its original size than the lower. When the added fluid was removed by aspiration and the surface of the heart dried by blotting, the deflections of both curves regained their original magnitude (Fig. 1 *C*). With one exception neither the direction nor the relative size of these deflections was

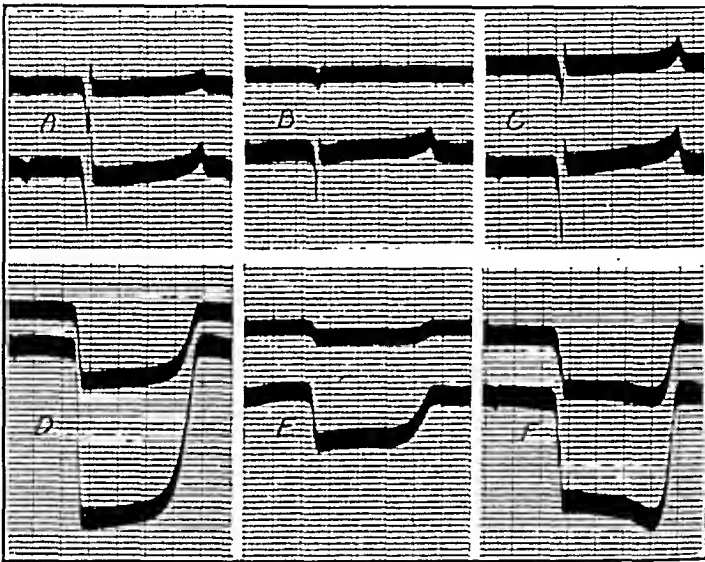


Fig. 1.—Experiment I. Exploring electrodes close together on ventral surface of turtle's ventricle. Indifferent electrodes 16 cm. from turtle (see text). Ordinate scale; lower curve, 5 mv. per centimeter; upper curve uncertain (see text). In all experiments the connections were so made that negativity of the exploring electrode produced an upward deflection in the corresponding curve. *A*, control; *B*, after immersing heart in 0.9 per cent NaCl; *C*, after removing saline and drying heart's surface; *D*, after burning tissue beneath exploring electrodes; *E*, after again immersing heart in saline; *F*, saline removed and heart dried.

altered either by flooding or by drying the heart. The upward deflection at the end of the QRS interval originally present in the lower curve was very much smaller in subsequent records. Since it did not regain its former size when the heart was dried, this change was probably due to a slight shift in the position of the y-electrode when fluid was poured over the heart.

The next step was to burn a small area immediately beneath the exploring electrodes with a hot iron. The ventricular complexes of both curves were immediately transformed into downwardly directed, monophasic deflections (Fig. 1 *D*). When the heart was flooded, the size of these deflections was greatly reduced, but their general outline was not changed (Fig. 1 *E*). The upper curve again fell off proportionately more than the lower. When the added fluid was removed, both curves increased in size, but neither quite regained its original amplitude or its original form

(Fig. 1 *F*). The appearance of a notch in each curve at the point where the chief upstroke or intrinsic deflection began before the heart was injured by burning should be noted.

In one respect this experiment was imperfect. When the first curves were taken, the tension of each galvanometer string was adjusted to give a deflection of 1 cm. for a potential difference of five millivolts. When the experiment was completed, however, it was found that the sensitivity of the galvanometer responsible for the upper curve was less than one-half the desired value. It is not known whether an error was made in adjusting the string tension or whether the sensitivity of this instrument fell off during the course of the experiment. The lesser size of the upper curve in the records taken when the heart was not immersed is, therefore, probably due to faulty standardization.

When fluid was poured upon the heart, the effective surface of the x-electrode, which was furnished with a bare wick, necessarily receded 2 or 3 mm. from the heart, and converted the previous direct lead into a semidirect lead. The effective surface of the y-electrode, which was rubber-tipped, also moved away from the heart, but the movement must necessarily have been very small. This difference between the two electrodes accounts for the proportionately greater reduction in the size of the upper curve when the heart was flooded. A similar difference between wick and rubber-tipped electrodes was observed in all experiments in which they were compared. Even when the heart has been blotted dry, some fluid clings to its surface and, in experiments of the kind under consideration, more soon collects. Rubber-tipped electrodes, which can be brought into more intimate contact with the muscle, are therefore likely to yield somewhat larger curves than wick electrodes unless care is taken to keep the surface of the heart as dry as possible.

Experiment II. In this instance the indifferent electrodes were placed on the tail. Both exploring electrodes were rubber-tipped, but the wicks extended approximately 1.5 mm. beyond the insulation. These electrodes were placed on the ventral surface of the exposed ventricle; the x-electrode near the base on the left side, and the y-electrode on the right side near the apex. The distance between them was about 13 mm. After some preliminary observations the surface of the heart was dried, and a set of control curves was taken (Fig. 2 *A*). When the heart was flooded to a depth of 5 mm., both curves became very much smaller (Fig. 2 *B*). The size of all the deflections was then doubled (Fig. 2 *C*) by reducing the tension of both galvanometer strings until a potential difference of ten millivolts produced a deflection of 4 cm. instead of 2 cm. As the fluid drained away, there was a further increase in their magnitude (Fig. 2 *D*), and when the heart was dried they became still larger (Fig. 2 *E*). Apart from these changes in amplitude both curves maintained their original outline; the direction and relative size of the various deflections remained the same throughout.

After repeating these observations another control curve (Fig. 2 *F*) was taken, and a small area (about 5 mm. in diameter) beneath the x-electrode was then burned. The ventricular complexes of the upper curve promptly became monophasic (Fig. 2 *G*), but it should be noted that the injury altered only those portions of the ventricular complex that occurred after the onset of the chief upstroke or intrinsic deflection. The shape of the downstroke that preceded this deflection was not changed; the monophasic curve is marked by a notch at the point where this downstroke ends. The change produced by the injury in the form of the lower curve was less pronounced but nevertheless definite. It consisted in a very distinct elevation of the RS-T junction and the RS-T segment. In general character these changes were not unlike those that took place in the upper curve, but they were smaller and in the opposite direction. When the heart was flooded with saline

(Fig. 2 *H*) and subsequently dried (Fig. 2 *J*), the size of both curves changed in the same manner as before. These procedures had no effect upon the general outline of either. When an electrode with a bare wick was substituted for the rubber-tipped x-electrode, flooding the heart produced a much greater reduction in the amplitude of the monophasic curve than it had before, but there was no other material difference.

In several experiments we studied the changes that occur in the responses of injured heart muscle with the lapse of time. It is, of course, well known that the monophasic responses produced by injuring the heart are transient. We wished particularly to determine whether T-wave changes similar to those seen in coronary occlusion occur when displacement of the RS-T segment produced by injuring the turtle's heart subsides. Because pronounced variations in the form of the T deflec-

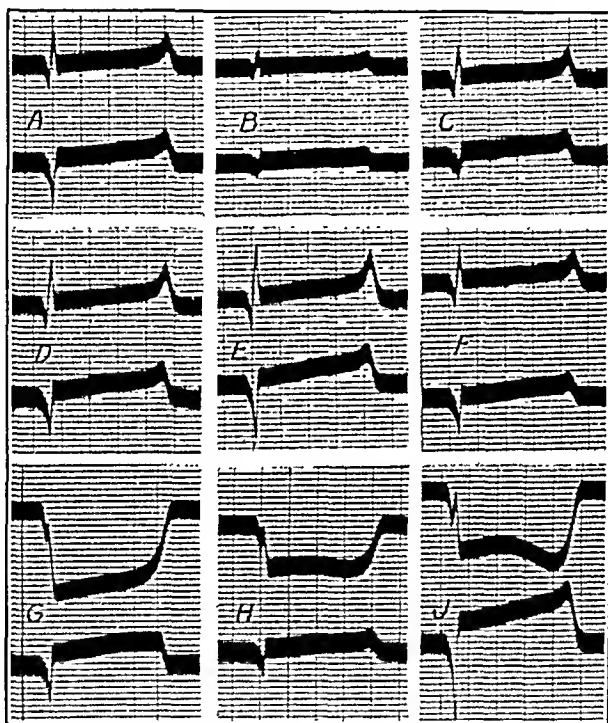


Fig. 2.—Experiment II. Exploring electrodes on ventral surface of turtle's ventricle. Indifferent electrodes on tail. Ordinate scale; records *A* and *B*, 5 mv. per centimeter; other records, 2.5 mv. per centimeter. *A*, control; *B*, after immersing heart in 0.9 per cent NaCl; *C*, after doubling sensitivity of both galvanometers; *D*, fluid draining away; *E*, remaining fluid removed and heart dried; *F*, second control; *G*, after burning tissue beneath x-electrode (upper curve); *H*, heart again immersed in saline; *J*, excess fluid removed and heart dried.

tion often occurred without obvious cause, we found it impossible to answer this question with certainty. Subsequent observations (Wilson, Johnston, Hill and Grout⁵) on dogs suggest that the inversion of the T deflection that follows elevation of the RS-T segment in clinical coronary occlusion is due to phenomena that take place at the margins of the infarcted area, and is not comparable to the minor T-wave changes that we sometimes observed after the disappearance of RS-T displacement produced by burning the surface of the cold-blooded heart.

Experiment III. The turtle was placed on its back in a shallow dish containing Ringer's solution, and the indifferent electrodes were 16 cm. from the heart. Both exploring electrodes were in contact with the ventral surface of the ventricle, the

x-electrode well toward the left, and the y-electrode on the right side. After taking a control record (Fig. 3 *A*) the exploring electrodes were temporarily removed, and the basal portion of the dorsal ventricular surface was burned. The curves taken immediately after replacing the electrodes in their original positions show a definite upward displacement of the RS-T junction and the RS-T segment (Fig. 3 *B*); in the upper curve this displacement is conspicuous, in the lower it is comparatively small. Subsequent records showed a gradual decrease in the displacement (Fig. 3 *C*), and after the lapse of fifteen minutes it practically disappeared. No further change occurred during the next half-hour (Fig. 3 *D*). At the end of this period the dorsal surface of the ventricle was burned again and over a slightly larger area than before. As a result the RS-T displacement returned (Fig. 3 *E*). No T-wave changes similar to those that are seen in myocardial infarction occurred.

Experiment IV. In some of the experiments in which one exploring electrode was directly in contact with the injured area the disappearance of the downward RS-T

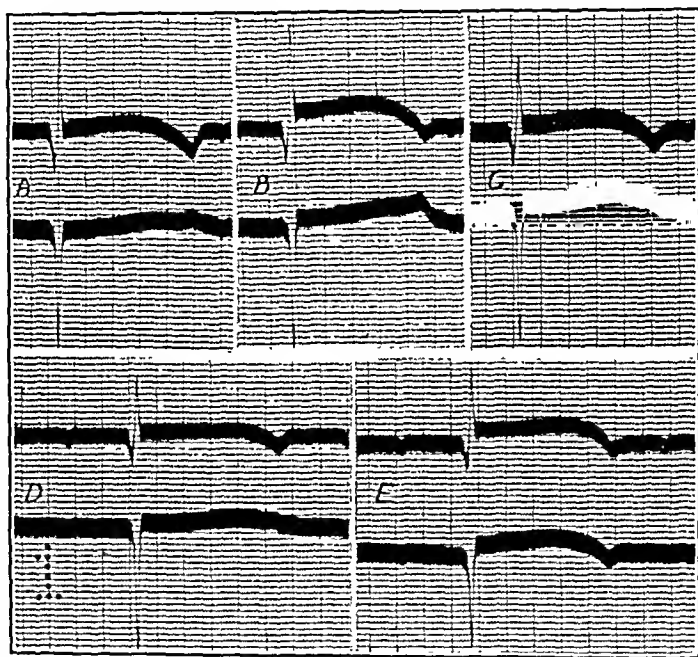


Fig. 3.—Experiment III. Exploring electrodes on ventral surface of turtle's ventricle. Indifferent electrodes 16 cm. from heart. Ordinate scale; 5 mv. per centimeter. *A*, control; *B*, after burning dorsal surface of ventricle; *C*, nine minutes after burn; *D*, forty-five minutes after burn; *E*, after second burn on dorsal surface.

displacement produced by the injury in the corresponding curve was accompanied by the development of a sharp upward movement at the end of the ventricular complex. This phenomenon is shown in the records reproduced in Fig. 4. In this experiment the heart was exposed by trephining the plastron, and the indifferent electrodes were placed within the trephine opening about 2 cm. from the heart. The exploring electrodes were in contact with the ventral surface of the ventricle, the x-electrode near the left margin of its basal, and the y-electrode near the right margin of its apical portion. After taking a control record (Fig. 4 *A*) a small area beneath the x-electrode was burned. The upper curve promptly became monophasic, and the lower showed a very slight elevation of the RS-T segment (Fig. 4 *B*). The monophasic deflection of the upper curve rapidly decreased in size (Fig. 4 *C*), and the initial deflections of the ventricular complex gradually regained their former shape (Fig. 4 *D*, *E* and *F*). In the control record the T deflection of the upper

curve ended in a distinct downward movement, but as the RS-T displacement of this curve diminished, a sharp peak developed at the point where this dip had formerly occurred (Fig. 4 *E*). The development of this peak was accompanied by the appearance of a simultaneous depression in the lower curve. In the last records (Fig. 4 *F*) this depression is not present, but it is possible that the position of the y-electrode shifted slightly during the latter part of the experiment. Although the T-wave change in this and in other similar experiments was in the same direction as that which occurs in coronary occlusion, it is doubtful whether it had a similar origin.

DISCUSSION

Apart from a slight difference in magnitude, the variations in potential at a given point on the ventral surface of the beating heart, when that surface is exposed to the air, are similar in all respects to the variations in potential in the immediate neighborhood of the same point when

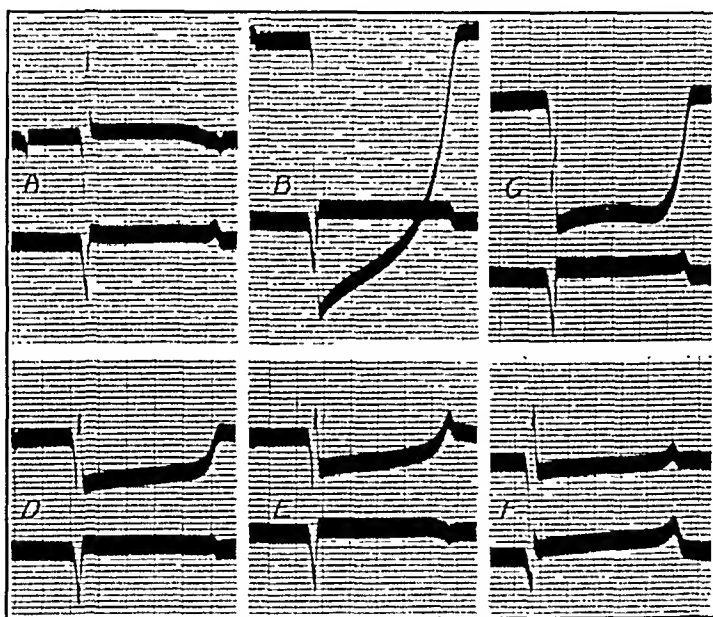


Fig. 4.—Experiment IV. Exploring electrodes on ventral surface of turtle's ventricle. Indifferent electrodes about 2 cm. from the heart. Ordinate scale; 5 mv. per centimeter. *A*, control; *B*, immediately after burning muscle beneath x-electrode (upper curve); *C*, four minutes after burn; *D*, fourteen minutes after burn; *E*, one hour after burn; *F*, four hours, forty-two minutes after burn.

the heart is completely surrounded by conducting material. In experiments of the kind under consideration it is certainly legitimate to neglect the potential variations of the distant electrode when the exploring electrode is very close to a portion of the heart's surface that is immersed. This cannot be denied without asserting that the laws which define current flow in volume conductors are invalid. We see no reason for considering the distant electrode appreciably less indifferent when the exploring electrode is in contact with a part of the heart's surface that is exposed to the air. We shall therefore assume that in all of our experiments the indifferent electrodes were at zero potential throughout the cardiac cycle.

If the potential of the distant electrode was not significantly affected by the heartbeat, the monophasic responses obtained in our experiments must be regarded as representing the potential of the exploring electrode and hence of the injured or dead muscle in contact with it.*

If we adopt the language of the membrane theory, we may say that when a small spot on the surface of the heart has been burned, the cell membranes of the superficial layers of muscle which have been killed are completely depolarized. We may assume that this dead tissue is bounded by a zone of injury in which the cell membranes are partially depolarized, and that the muscle beyond this zone is in no way affected. Any difference in potential between our electrodes produced by the current of injury may be neutralized. So far as the particular lead we are using is concerned this procedure restores the electrical conditions that prevailed before the injury. By compensating the injury current we have in effect repolarized the dead and injured tissues to the original intensity. The injury can now have no effect upon the potential difference between our electrodes until an excitation wave reaches the injured region. When the excitatory process spreads over the heart, partial or complete depolarization of the uninjured cell membranes takes place, and we shall assume that the resulting change in the electromotive force across these membranes is everywhere uniform. The excitation wave cannot, however, alter the electromotive force across the cell membranes that have been destroyed; in the zone of injury the degree of depolarization produced by its arrival may vary from zero to normal.

The injury cannot modify the electrical effects produced by the excitation of parts of the heart that it does not involve. When the exploring electrode is in contact with the ventricle, the chief upstroke or intrinsic deflection of the curve obtained signals the arrival of the excitatory process at the subjacent epicardial surface (Lewis and Rothschild⁷). Since a local injury can have no effect upon the action current until the excitation wave reaches the injured region, the deflections of this curve that precede the chief upstroke are not changed by superficial injuries affecting the muscle immediately beneath the exploring electrode.

*Physiologists have usually obtained curves of this kind by placing both electrodes upon the epicardial surface, one upon an uninjured and the other upon an injured region. Failing, for the most part, fully to appreciate that the potential of an electrode on the heart is affected not only by the excitation of the muscle immediately in contact with it, but also by the excitation of every other part of the heart, they have generally assumed that because dead muscle can produce no action currents, the potential of the latter electrode does not change. They have therefore regarded the curve obtained as representing the potential variations of the electrode in contact with uninjured muscle. Since the potential of a given point can be measured only with reference to that of some other point, one is at liberty to choose the standard of reference that is most suitable for his purpose. In studying an electric field it is, however, conventional to define the absolute potential of any point in the field as its potential with reference to that of a point outside the field (Attwood⁸). For many reasons, some of which we have already given, we have found it desirable when studying the electric field produced by the heartbeat to choose as our zero the potential of a point as far from the heart as possible.

The most striking effects of a fresh injury occur during the period immediately after all the uninjured cardiac muscle has passed into the excited state. Assuming that the current of injury has been neutralized, the potential of the exploring electrode at this time must be the same as it would be if the cell membranes of the dead muscle remained in the resting and fully polarized state and those of the injured muscle were only partially depolarized. The excitation wave is blocked at the boundaries of the injured tissue. The electric forces produced by its spread at the moment when, and in the region where, block occurs persist unaltered until they are extinguished by the return of the excited muscle to the resting state.*

It is possible to obtain a more exact idea of the electrical situation in the following way: Consider the zone lying between the two surfaces which separate the injured muscle from the dead muscle on the one side

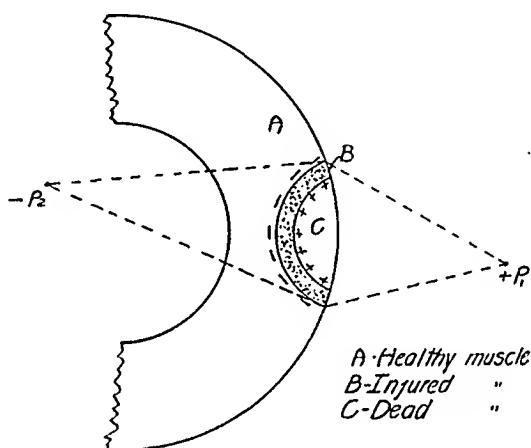


Fig. 5.—Diagrammatic representation of the electric field produced by an injured section of the ventricular wall at the end of the QRS interval. This field is similar to the one that would be produced if the injured muscle (dotted zone) were polarized in the sense indicated. If the exploring electrode were placed at P_1 , the RS-T displacement would be downward; if this electrode were placed at P_2 , the displacement would be upward.

and from the uninjured muscle on the other. Imagine that each fiber element within this zone is polarized in such a sense that the end nearest the dead muscle is positive and the end nearest the uninjured muscle negative. Imagine further that the intensity to which each element is polarized is equal to the difference between the change in the intensity of polarization of the cell membranes of that element actually produced by the spread of the excitation wave over it and the change that would have been produced if no injury had occurred. The electric field produced by this polarized zone (see diagram, Fig. 5) will then be identical with the one that occurs at the end of the QRS interval when the excita-

*Displacement of the RS-T segment may, of course, occur even when the injury is not severe enough to cause block. It becomes maximal when block is produced. For the production of this phenomenon it is essential that, in the region affected, the change in the intensity of membrane polarization produced by excitation shall be less than elsewhere. Whether a current of injury is or is not flowing is immaterial.

tion wave has been blocked at the boundary of the injured region.* For many purposes we may neglect the width of the zone specified and replace it by a single polarized surface lying between the injured and the uninjured tissue. At each point of this surface the intensity of polarization must be such as to make the drop in potential across it equal to the drop in potential across the corresponding portion of the polarized zone, and this in turn must be equal to the difference between the change in the electromotive force across the cell membranes produced by excitation on one boundary of this zone and that produced on the other. The character of the electrical field that would be produced by such a polarized surface has been discussed elsewhere.³ For our present purpose we may regard the potential at a given point as roughly proportional to the product of the intensity of polarization† and the solid angle subtended at that point by any surface having the same boundaries or edges as the one specified (Wilson, Macleod and Barker³).

For a short period immediately following the QRS interval we may therefore expect the potential of the exploring electrode to be the same as it would be if the surface separating injured and uninjured muscle were polarized in the sense and to the intensity designated. If the exploring electrode is in contact with the injured area, the displacement of the RS-T segment will be downward; and if the surface of contact between the heart and the electrode lies wholly within the boundaries of the injured area, the size of the latter will have little or no effect upon the amount of displacement. If the heart is immersed in a conducting fluid and the exploring electrode is gradually moved away from the injured region along a line perpendicular to the surface of the heart, the solid angle subtended at the electrode by the polarized surface specified will decrease and the downward displacement of the RS-T segment must diminish. It should decrease much more rapidly when the injured area is small than when it is large. In order to produce RS-T displacement when the exploring electrode is at a considerable distance from the heart a large area of injury is necessary. If the injury is on the epicardial surface and the exploring electrode is on the opposite side of the heart, the solid angle subtended at this electrode by the polarized surface specified will be negative and the RS-T displacement will be upward.

By appropriate means a grade of injury insufficient to kill the muscle most seriously affected may, of course, be produced. If the excitation wave is not prevented from reaching this muscle, the drop in potential across the postulated surface between injured and uninjured muscle

*See Wilson, Macleod and Barker.³

†To avoid unnecessary complications we assume that the intensity of polarization over the surface in question is uniform. The fact that this is not necessarily the case does not affect the conclusions here set forth.

will not be so great as it would be if block occurred. The RS-T displacement cannot be maximal and a pure monophasic response cannot occur unless the injury is of sufficient grade to make it impossible for the excitation wave to reach the most severely injured tissue. If the injury is slight, the RS-T displacement will be slight; other factors being equal its magnitude should be proportional to the effect, in the zone where it is most intense, upon the change produced by excitation in the electromotive force across the cell membranes.

Only fresh injuries produce RS-T displacement. Within a short but variable time conditions similar to those that obtained before the injury are reestablished. The fatally injured muscle dies; some of the damaged cell membranes recover; new membranes may perhaps form. During this period of recovery the curves obtained are similar in every way to those that would be obtained if the grade of injury gradually grew less. The electrical effects produced by the tissue that has been killed are, of course, permanently lost.

SUMMARY

When an electrode at a distance from the heart is paired with an exploring electrode in contact with the ventricular surface, the curve obtained represents the potential variations of the latter. By comparison the potential variations of the former are so small that they may be neglected.

The curve obtained from a given point when the ventricular surface upon which the exploring electrode is placed is exposed to the air is larger but similar in all other respects to that obtained from the same point when the heart is completely surrounded by a conducting medium.

When the muscle beneath the exploring electrode is injured, pronounced displacement of the RS-T segment occurs and the ventricular complex often becomes monophasic. If the connections have been made so that relative negativity of the exploring electrode produces an upward deflection, the direction of this displacement is downward. When the subepicardial muscle is injured over a large area and the injury and the exploring electrode are on opposite sides of the heart, the displacement is upward and is less pronounced.

At the time when the displacement is maximal the electric field about the heart is similar to the one that would be produced if the surface between the injured and the uninjured muscle were polarized in such a sense as to make the injured muscle positive. A local injury on the epicardial surface does not alter the action current produced by portions of the heart that the injury does not involve. In any lead the deflections that are written before the excitation wave reaches the injured region are of the same form after the injury as before. The RS-T displacement produced by burning the surface of the cold-blooded heart quickly

subsides and is not, apparently, followed by T-wave changes of the kind that occur when the mammalian heart is injured by coronary ligation.

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THE INTERPRETATION OF THE GALVANOMETRIC CURVES
OBTAINED WHEN ONE ELECTRODE IS DISTANT FROM
THE HEART AND THE OTHER NEAR OR IN CONTACT
WITH THE VENTRICULAR SURFACE*

PART II. OBSERVATIONS ON THE MAMMALIAN HEART

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INTRODUCTION.—The observations reported here supplement those described in Part I.‡ The point of view is fundamentally the same, but the method of analysis is different. Our present purpose is to discuss certain relations between the potential variations that occur at or near the epicardial surface of the mammalian heart and those that take place inside the ventricular cavities. Our investigation of this subject was prompted by the observation that when the anterior wall of the heart is infarcted, the ventricular complexes in precordial leads are similar to those obtained when the exploring electrode is placed opposite one of the valvular orifices of the normal heart.¹ We suspected that in both cases the ventricular complexes were of the kind that would be obtained by placing this electrode inside the ventricular cavity.

Methods.—Practically all the observations discussed on the following pages were made more or less incidentally in the course of a series of experiments in which our main object was to study the electrocardiographic changes produced by infarction of the myocardium. The dogs used had previously been subjected to an operation in which coronary ligation was performed or attempted. There is, however, no reason to believe that different results would have been obtained if normal animals had been used. We shall consider no observations upon which the previous interference or attempted interference with the coronary circulation could conceivably have a bearing. Unless otherwise noted all observations were made after exposing the heart by splitting the sternum and opening the pericardial sac. Standard Lead I was taken simultaneously with all direct and semidirect leads. The latter were taken with the galvanometer responsible for the lower curve, and this galvanometer was connected to the plate circuit of a vacuum tube as in the case of the turtle experiments described in Part I.

The indifferent electrode was usually placed upon the left hind leg; in a few experiments a central terminal, connected to the two forelegs and to the left hind leg through resistances of 5,000 ohms, served as the indifferent point.² For direct leads the string tension was adjusted to give a deflection of one-half centimeter when a potential difference of ten millivolts was introduced into the input circuit.

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‡See page 163.

When semidirect leads were taken, the deflection per millivolt was greater, but the galvanometer sensitivity varied with the position of the exploring electrode. The exploring electrodes used were similar to those employed in our turtle experiments (Part I), except that in most instances the wick was replaced by a small piece of sponge. To obtain records of the potential inside the ventricular cavities we employed an electrode that could be thrust through the heart wall. This stab-electrode, which was also useful in studying the responses of injured heart muscle, consisted of a piece of heavy copper wire, about three inches long, sharpened at the end. Enamelled wire was used and the insulation was left intact to within approximately one millimeter of the point. Because of the high resistance in the input circuit of the vacuum tube this electrode did not polarize.

Illustrative experiment.—The curves reproduced in Fig. 1 are from an experiment (Experiment 45) in which a stab-electrode was pushed through the skin, in the fifth intercostal space 6 cm. to the left of the

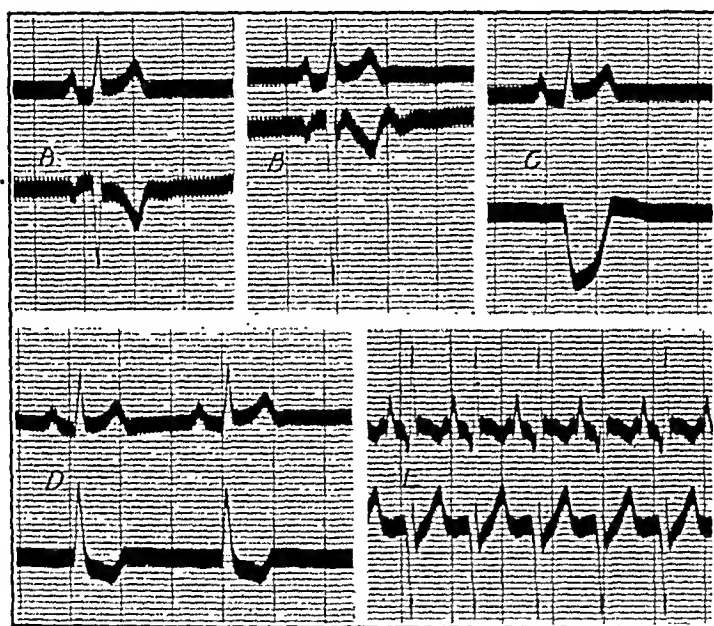


Fig. 1.—Experiment 45. Upper curve represents standard Lead I in all records. Lower curves obtained by pushing a sharp electrode, insulated to the tip, through the skin of the precordium (fifth interspace) and thrusting it deeper step by step until it entered the cavity of the left ventricle. A central terminal (see text) served as the indifferent point. A, electrode 0.75 cm. beneath the skin; B, electrode 2 cm. beneath the skin; C, electrode 3.75 cm. beneath the skin and just touching the heart; D, electrode 4.6 cm. beneath the skin and inside the cavity of the left ventricle. Ordinate scale of lower curves: A and B, 2 mv. per centimeter; remaining curves, 20 mv. per centimeter. In all experiments the connections were so made that negativity of the exploring electrode produced an upward deflection.

midline, and thrust step by step through the underlying tissues until it entered the cavity of the left ventricle. This procedure was carried out after the animal had been fully anesthetized and while the chest was intact. The indifferent point was a central terminal of the kind already described. Curves were taken when the uninsulated point of the electrode was 0.75 cm. beneath the skin (Fig. 1 A), 2.0 cm. beneath the skin (Fig. 1 B), 3.75 cm. beneath the skin and just touching the heart (Fig. 1 C), and 4.6 cm. beneath the skin and in the cavity of the left ventricle

(Fig. 1 *D*). For the first two curves the galvanometer sensitivity was one-half normal; for the last two it was one-twentieth normal. The chest was then opened, and when the heart was exposed, the puncture wound made by the sharp electrode was easily located on the anterior surface of the left ventricle about 1 cm. below the interventricular groove. A curve was then taken with a sponge-tipped exploring electrode placed directly over this point (Fig. 1 *E*).

These curves are of interest from several points of view. We may call attention, first of all, to the close resemblance in general outline between the initial ventricular deflections of the curves taken when the stab-electrode was still some little distance from the heart and the initial deflections of the curve taken from the region of the puncture wound after the heart had been exposed. The T deflections of the former curves and those of the latter are quite unlike, but this is not surprising since it is known that the T deflection is easily modified by many factors. When the stab-electrode came in contact with the heart, the resulting injury, which must have involved a very small amount of muscle, gave rise to a monophasic ventricular complex. Because the injured area was smaller than the surface of the sponge-tipped electrode, and also perhaps because of the lapse of time, no definite RS-T displacement was observed when this electrode was later placed in contact with the wound.

The potential of the ventricular cavities.—The curve from the left ventricular cavity (Fig. 1 *D*) is smaller in amplitude but otherwise similar to those obtained from this cavity in experiments in which the heart had been exposed. The main upstroke occurs very early and is not preceded, as is invariably the case in epicardial curves, by a downward movement. It is less abrupt and of longer duration than the intrinsic deflections of epicardial leads. The T deflection is represented by a rounded depression. The curves obtained from the cavity of the right ventricle frequently show a small initial dip; in other respects they are similar to those obtained from the cavity of the left.

The curves reproduced in Fig. 2 (*A*, *B*, *C*, and *D*), represent the potential variations of the two ventricular cavities before and after the left branch of the His bundle was cut (Experiment 26). Between the two curves taken before branch block was produced there is only one important difference; the main upstroke of the right ventricular curve (Fig. 2 *A*) is preceded by a small inverted peak, but the left ventricular curve (Fig. 2 *C*) shows no more than a mere trace of such a deflection. When the bundle was cut the former curve lost its inverted peak (Fig. 2 *B*), and the latter developed a large downward movement (Fig. 2 *D*), which completely altered its appearance. In experiments in which the right branch of the His bundle had been cut the right ventricular curve

began with a large downward movement (Fig. 2 *E*), and the first deflection of the left ventricular curve was upward (Fig. 2 *F*).

We believe that these observations have an important bearing upon the interpretation of all curves obtained by placing the exploring electrode near or in contact with the epicardial surface. The electromotive force produced by the excitation wave as it spreads over the ventricular walls from within outward tends to make the ventricular cavity negative and the epicardial surface positive. The magnitude of the electromotive force generated by any section of the ventricular wall at a given instant is measured by the difference between the electromotive force across the cell membranes of the innermost and the electromotive force across the cell membranes of the outermost layers of muscle (Wilson, Macleod

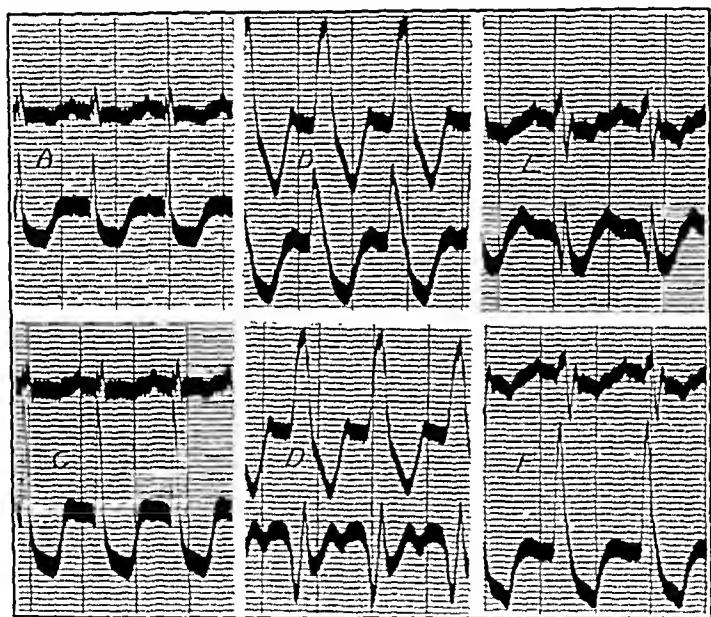


Fig. 2.—Upper curve represents standard Lead I. Lower curves as follows: Potential of right ventricular cavity before (*A*) and after (*B*) cutting the left branch of the His bundle. Potential of left ventricular cavity before (*C*) and after (*D*) cutting left branch of His bundle. Potential of right (*E*) and potential of left (*F*) ventricular cavity after cutting the right branch of the His bundle. The last two curves are from Experiment 50; the others are from Experiment 28. In both these experiments a central terminal served as the indifferent point.

and Barker³). Before activation of the subendocardial muscle begins and after activation of the subepicardial muscle is completed, the electromotive force across the ventricular wall is zero. It increases rapidly when the excitation reaches the endocardial and decreases rapidly when it reaches the epicardial surface. Throughout the QRS interval the electric field about the heart is equivalent to that which would be produced if the zone of muscle undergoing activation were polarized in such a way as to produce an electromotive force between its boundaries equal to that generated by the corresponding portion of the ventricular wall.³

The curve from the left ventricular cavity reproduced in Fig. 1 *D*

represents the potential at a point a little less than 1 cm. away from the puncture wound on the epicardial surface. Nevertheless its initial deflections are very different from those obtained, after the heart had been exposed, by placing the exploring electrode directly over this wound. If we may neglect the effect of exposing the heart upon the electric field in this neighborhood, we may say that throughout the period when the potential of the epicardial surface was positive, that of the nearest part of the ventricular cavity was negative.

We believe that all the major differences between the initial deflections of the two curves in question must be ascribed to the effect of the electromotive forces generated by the activation of that section of the ventricular wall through which the stab-electrode passed. This opinion is based, first of all, upon the character of the laws that define the flow of electric currents in volume conductors.³ Electromotive forces generated in other parts of the heart might easily produce a difference in potential between two electrodes on opposite sides of the lateral wall of the left ventricle and approximately 1 cm. apart. It would be practically impossible for such forces to make one of these electrodes negative and the other positive with respect to a point distant from the heart. The initial deflections in Fig. 1 *E* are, as we have already pointed out, strikingly similar in general outline to those in Figs. 1 *A* and 1 *B*, which represent the potential at two points, one approximately 1.75 cm. and the other 3 cm. from the puncture wound. The potential variations that occurred at these points during the QRS interval differed only in magnitude from those that took place at the epicardial surface. The reason must be that between these points and the epicardial surface there was no cardiac muscle generating an electromotive force. Finally, it was found in the course of our observations on experimental myocardial infarction that when a section of the ventricular wall has been killed, the curves obtained by leading from the epicardial surface and those obtained by leading from the nearest part of the ventricular cavity are practically identical in form.⁴ It is, therefore, clear that the potential of a point just inside and that of a point just outside a given part of the ventricular wall vary in a similar way when no electromotive force is being generated by the muscle between them.

When the excitation wave has spread over most of the subendocardial muscle of the left ventricle, we may think of the cavity of this ventricle as surrounded by a zone of muscle undergoing activation and producing effects similar to those that would occur if it were electrically polarized. For most purposes the width of this zone may be neglected, and it may be regarded as a polarized surface. At any instant during the QRS interval there must be in this polarized zone or surface certain windows or openings: an opening corresponding to each of the valvular orifices; to each region where the subendocardial muscle has not yet been acti-

vated; and to each region where the whole thickness of the ventricular wall has passed into the excited state. Throughout the QRS interval, points in the ventricular cavity lie on the negative side of the polarized zone and display a negative potential. The potential of a point on or near the epicardial surface and opposite a window must be similar to that of the neighboring part of the ventricular cavity. We may therefore expect an exploring electrode that is on or near the epicardial surface to be either at zero potential or negative with respect to a distant point until the subendocardial muscle of the subjacent wall is activated. When activation of this muscle begins, the potential of this electrode will rapidly become less negative or more positive; as soon as this muscle is fully active it will be strongly positive. When the excitation wave reaches the subepicardial muscle, the potential difference between the epicardial surface and the ventricular cavity will rapidly decrease; when this muscle is fully active, it will practically disappear, and the exploring electrode will again be either negative or at zero potential with respect to an indifferent point.

In this discussion we have, for the sake of simplicity, neglected the effects produced by the simultaneous spread of the excitation wave through the walls of the right ventricle. The cavity of this ventricle will likewise be surrounded by a polarized zone or surface, which must produce an electric field and affect the potential of points on the epicardial surface of the left ventricle as well as elsewhere. When both sides of the septum are activated simultaneously, however, we may neglect the effects produced by it, and regard the two polarized surfaces as forming a single surface surrounding both ventricular cavities. If the two sides of the septum are not activated simultaneously, the matter is more complicated. In bundle-branch block the cavity of the homolateral ventricle lies outside the polarized zone which surrounds the cavity of the contralateral ventricle, and is therefore positive until the excitation wave has pierced the septum. The inverted peak that usually precedes the main upstroke in curves from the right ventricular cavity of normal animals apparently means that the left side of the septum is ordinarily excited in advance of the right.

Epicardial curves.—We may now apply the principles outlined to the interpretation of the more common types of initial ventricular deflections obtained by leading directly from the epicardial surface. Examples of these are shown in Fig. 3 (*A, B, C, and D*). Leads from the central portion of the anterior surface of the right ventricle, where the muscle is thin, usually yield curves which show a small downward movement followed by the intrinsic deflection,⁵ which rises far above the baseline (Fig. 3 *A*). We ascribe the downward movement to the electrical effects produced by the passage of the excitation wave outward through the thin

wall.* As soon as the subepicardial muscle beneath the exploring electrode has become fully active, this electrode assumes the potential of the ventricular cavity which at that instant (very early in the QRS interval) is strongly negative.

It is true that the onset of the intrinsic deflection marks the arrival of the excitation wave at the epicardial surface.⁵ This deflection is not, however, due to electric forces produced by and originating in the muscle beneath the exploring electrode. If the excitation wave were not spreading on the opposite side of the ventricular cavity, the complete activation of this muscle might permit the string to return to the baseline, but could not carry it beyond. The electric forces that make the exploring electrode strongly negative and raise the intrinsic deflection above the

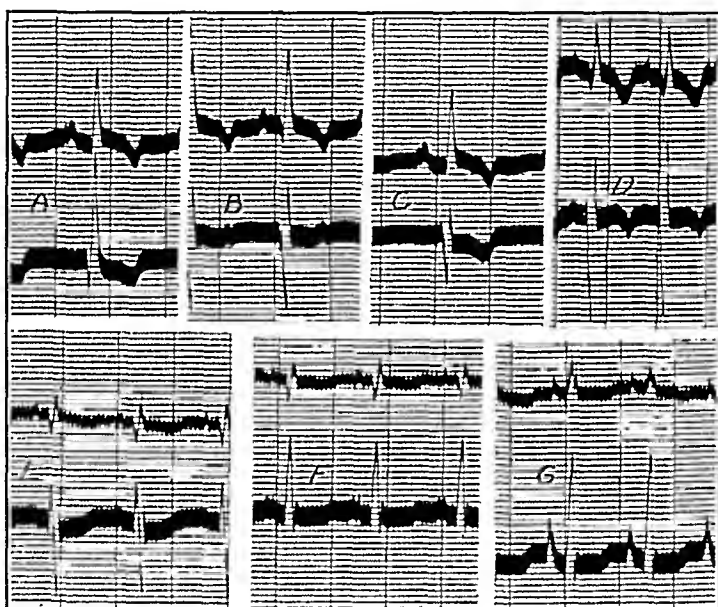


Fig. 3.—Upper curve represents standard Lead I in all records. The data given below refer to the lower curves only.

Records of upper row: Exploring electrode on the epicardial surface. *A*, exploring electrode on right ventricle (central region); *B*, on left ventricle (near interventricular sulcus); *C*, on left ventricle (central part of ventral surface); *D*, on left ventricle (near apex). The first three of these curves are from Experiment 50, in which a central terminal served as the indifferent point. The last one is from Experiment 32 in which the indifferent electrode was on the left hind leg. Ordinate scale: 20 mv. per centimeter.

Records of lower row. Curves from an experiment, performed in January, 1930, in which the indifferent electrode was placed on the left hind leg. *E*, exploring electrode on conus arteriosus just below pulmonary valve; *F*, exploring electrode on pulmonary artery just above pulmonary valve; *G*, exploring electrode in cavity of right auricle. Ordinate scale: for *E*, 10 mv. per centimeter; for *F* and *G*, 5 mv. per centimeter.

zero level are the same as those that make the ventricular cavity strongly negative. These forces originate, for the most part, in muscle distant from the exploring electrode.

*The same forces that produce the initial downward movement in curves from the right ventricular cavity may contribute in some small measure to the formation of this deflection.

In curves from the thicker portions of the right and from the greater part of the left ventricular surface the intrinsic deflection is preceded by a downstroke that is much deeper and of longer duration (Fig. 3 *B*). The greater duration of this deflection, in comparison with those obtained from thin portions of the ventricular wall, is clearly due to the increased time required by the excitation wave to spread from the endocardial to the epicardial surface. Its greater depth may be due to several causes. Up to a certain point an increase in the thickness of the ventricular wall may tend to increase the electromotive force which it develops during activation. Excitation is not instantaneous, but requires a short interval of time. When the time required by the excitation wave to cross the ventricular wall becomes greater than the time necessary for complete activation of a single muscle element to take place, the endocardial surface must become fully active before activation of the epicardial surface begins, and the electromotive force between the two surfaces must reach its maximal value. It should be remembered, however, that the electromotive force across the ventricular wall is approximately equal to the difference in potential between the cavity and the epicardial surface. Early in the QRS interval the ventricular cavity is strongly negative; an electromotive force across the ventricular wall sufficiently large to produce a small downward deflection in a given epicardial lead at this time would produce a much larger one later when the negativity of the ventricular cavity is less pronounced. Intrinsic deflections that occur late do not rise far above the baseline because the potential of the ventricular cavity is then approaching zero. At a time when the potential of the cavity is not changing rapidly, the height of the intrinsic deflection, measured from the point below the baseline where it begins to the point above the baseline where it ends, may be taken as a rough measure of the electromotive force that existed across the ventricular wall immediately before its onset.

From some parts of the left ventricle, less often from parts of the right, curves are sometimes obtained in which the downward movement produced by the outward progress of the excitation wave is preceded by a small summit (Fig. 3 *C* and *D*). An unusually large deflection of this kind is shown in Fig. 3 *E*. This curve was obtained by leading from the epicardial surface of the conus arteriosus just below the pulmonary valve. The curve shown in Fig. 3 *F* was obtained from the surface of the pulmonary artery just above the valve, and that reproduced in Fig. 3 *G* from the cavity of the right auricle. The last two are similar to curves from the ventricular cavities; they show no distinct downward movement preceding the main upstroke. In the one instance the exploring electrode was opposite the pulmonary orifice and in the other opposite the tricuspid orifice, and in both cases its potential apparently varied with that of the right ventricular cavity. When this electrode was placed on the

muscle of the conus (Fig. 3 *E*), its potential followed that of the cavity only until the endocardial surface became active.* It then became positive and remained so until the excitation wave reached the epicardial surface, at which time the usual intrinsic deflection occurred.

We attribute the occurrence of an initial upward deflection that precedes the chief downward movement in epicardial leads to late activation of the endocardial surface. We believe that the summit of this deflection occurs approximately at the time when activation of this surface begins. In rare instances this peak is preceded by a diminutive downward movement, and the cause of this preliminary dip is obscure except in those cases where a similar and simultaneous dip occurs in leads from the ventricular cavity.

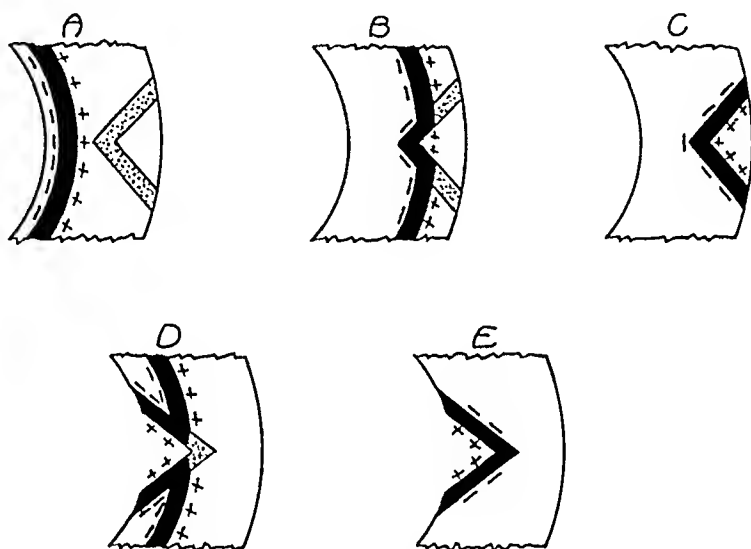


Fig. 4.—Diagrammatic representation of the electric forces generated by activation of a section of the ventricular wall that has been injured by pressing a sharp electrode against its epicardial (*A*, *B*, and *C*) or endocardial (*D* and *E*) surface. The dotted zone represents injured muscle (about the end of the sharp electrode) which the excitation wave has not yet reached. The black zone represents the uninjured muscle that is undergoing activation and the injured muscle which the excitation wave has reached and in which it has been blocked. Across this zone there is an electromotive force of the kind indicated. *A*, the electric forces early in the QRS interval before the excitation wave has reached the injured tissue; *B*, and *D*, just after the excitation wave has reached the injured tissue; *C* and *E*, at the end of the QRS interval when all of the uninjured muscle has passed into the excited state. For the sake of clarity the black zone has been made relatively narrow in comparison with the thickness of the ventricular wall; it is probably much wider than is here indicated.

The curves obtained when a sharp electrode is used.—Injuries that involve the subepicardial muscle over a small area have no appreciable effect upon the curves obtained by leading from the ventricular cavity; they have a very profound effect upon those obtained by leading directly from the region injured. When the curve reproduced in Fig. 1 *C* is compared with that shown in Fig. 1 *D*, it is clear that, in effect, the injury inflicted by the stab-electrode maintained throughout the greater part of systole the electromotive force generated across the subjacent

*In many animals leads from the conus yield curves in which the initial deflection is downward.

ventricular wall by the outward passage of the excitation wave. The reasons for this have already been given (Part I), but they may be restated in a somewhat different form. When the excitation wave is blocked at the boundary of the injured region, the effect is the same as if the muscle beyond the block were uninjured and remained in the unexcited state. The polarized zone which represents muscle undergoing activation spreads outward to the region of block and remains there until it is abolished by the return of the adjacent uninjured muscle to the resting condition (Fig. 4). At the end of the QRS interval, when all the uninjured muscle has been activated, the electromotive force across this zone is the same as if it were bounded on the outer side by

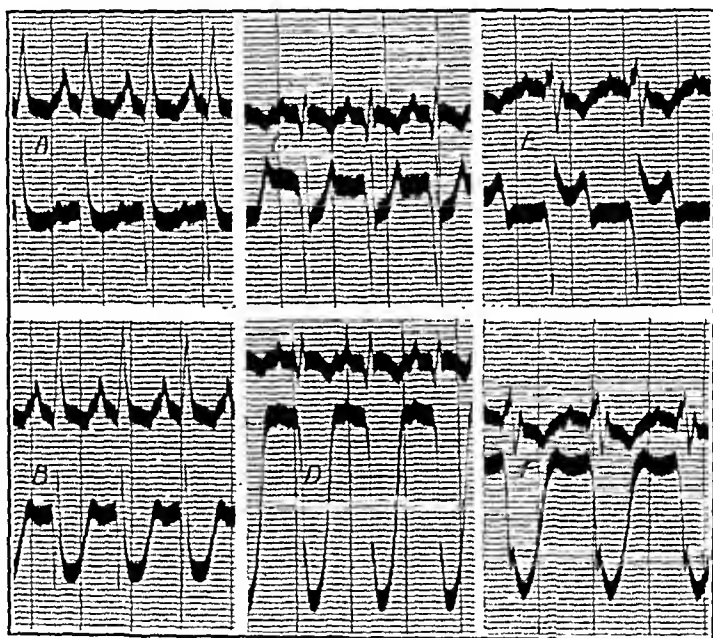


Fig. 5.—Upper curves represent standard Lead I in all records. The lower curves in the two records of each column were taken from the same or from neighboring points, one with a soft-tipped electrode (upper row) and the other with a sharp electrode (lower row). Ordinate scale: 20 mv. per centimeter. *A* and *B* are from the right central region (Experiment 15); *C* and *D* are from the ventral surface of the right ventricle, near the base (Experiment 11). *E* and *F* are also from the ventral surface of the right ventricle, near the base (Experiment 50) and were taken after the right branch of the His bundle had been cut.

resting and on the inner side by fully active muscle; it is therefore equal to the maximal electromotive force that the ventricular wall can generate between its two surfaces.

If the injury is not severe enough to cause block, it does not prevent the excitation wave from reaching the epicardial surface. It does not, therefore, abolish but merely reduces the decrease in the electromotive force across the ventricular wall that ordinarily follows this event. The effect is the same as if the subepicardial muscle could be partially, but not fully excited. The electromotive force across the polarized zone

bordering the injured muscle at the end of the QRS interval is then submaximal.

When two curves are taken from the same or from neighboring points on the epicardial surface, the first by means of a soft-tipped and the second by means of a stab-electrode, the ventricular deflections of the two curves are usually identical or nearly so up to the point where the intrinsic deflection begins (Fig. 5). The reason for this is obvious; as we have already pointed out (Part I), an injury cannot modify ventricular deflections that are written before the excitation wave reaches the injured tissue. The effect of the injury upon the intrinsic deflection varies with the grade of injury produced. With increasing grades of

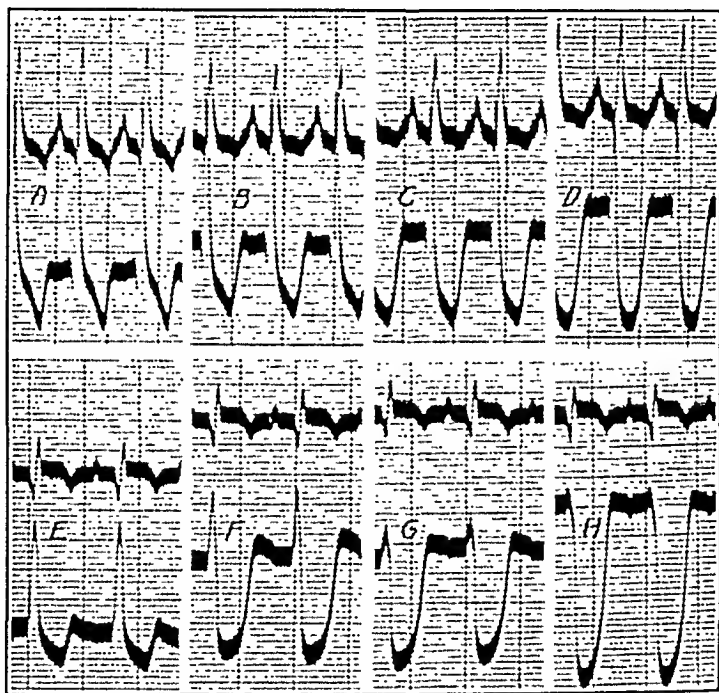


Fig. 6.—Upper curve standard Lead I throughout. Ordinate scale of lower curves: 20 mv. per centimeter. Upper row; *A*, from right central region with soft-tipped electrode; *B*, *C*, and *D* are from a nearby point and show the effect of using a sharp electrode and gradually pressing it more firmly against the heart (Experiment 45). Lower row: *E*, stab-electrode in left ventricular cavity (Experiment 44); *F*, point of electrode thrust into subendocardial muscle of dorsal wall; *G*, electrode thrust more deeply into dorsal wall; *H*, electrode thrust still more deeply into dorsal wall.

injury the sharp upward movement that constitutes this deflection becomes smaller and smaller; when the injury is sufficiently severe, it frequently disappears. The RS-T displacement also depends upon the grade of the injury, and presumably becomes maximal when the injury is sufficiently intense to block the excitation wave. A series of curves illustrating the effect of pressing a stab-electrode more and more firmly against the heart is shown in Fig. 6 (*A*, *B*, *C*, and *D*). These curves are from the central region of the right ventricle. The first (Fig. 6 *A*) was taken with a sponge-tipped electrode, the last three with a stab-electrode.

As the pressure upon the sharp electrode was increased, the intrinsic deflection became smaller and the RS-T displacement larger, and the increase in the latter was approximately equal to the decrease in the former (Fig. 6, *B*, *C*, and *D*).

When the intrinsic deflection rises high above the baseline, the injury inflicted by the stab-electrode seldom if ever abolishes it. Except during periods when the electromotive force across the ventricular wall is changing, the potential of a point on the epicardial surface and that of the neighboring portion of the ventricular cavity must vary together and in a similar way. When the curve from the ventricular cavity is rising, a curve from the epicardial surface must also rise unless the electromotive force across the intervening ventricular wall is increasing. Very soon after the excitation wave arrives at the zone of injury produced by a stab-electrode pressed against the epicardial surface, the electromotive force across the ventricular wall at this point must either diminish or become constant. If at that time the curve from the ventricular cavity is rising, the curve from the injured region must also rise. For this reason curves from an injured area on an epicardial region that normally displays an early intrinsic deflection almost always show a prominent notch or an upward movement early in the QRS interval.

We may look at this matter from another standpoint. As we have already pointed out, intrinsic deflections that rise above the baseline do so in response to electric forces originating in muscle distant from the region where they are recorded. An injury in this region cannot alter these forces. Nevertheless, if the injury is sufficient to block the excitation wave and does not involve the endocardial surface, so that the maximal electromotive force which the excitation wave is capable of producing is generated between the stab-electrode and the ventricular cavity, the upward movement produced by these distant forces should theoretically fail to carry the string beyond the zero level. Intrinsic deflections of the kind under consideration are, however, usually obtained in regions where the ventricular wall is thin, and it is possible that any injury sufficiently intense to block the excitation wave usually causes some depolarization of the cell membranes on the endocardial surface. This would tend to prevent the electromotive force across the ventricular wall from reaching its maximal value, and might make it impossible for the injury either to prevent the intrinsic deflection from rising above the baseline or to produce maximal RS-T displacement. When all the muscle lying between the electrode and the endocardium is killed, the potential of the exploring electrode is nearly the same as that of the ventricular cavity throughout the cardiac cycle.⁴ This situation often arises in myocardial infarction, both in animals and in man.

Curves of an interesting type are obtained when the stab-electrode is pushed through the ventricular cavity into the subendocardial muscle of

the posterior wall or of the septum. The first deflection of these curves is a prominent summit (Fig. 6 *F*), which becomes smaller if the electrode is pushed more deeply into the muscle (Fig. 6 *G* and *H*). Curves of the same kind are obtained if the electrode is thrust into the ventricular cavity and then withdrawn until its uninsulated point is beneath the endocardium. The potential of the electrode naturally varies with that of the ventricular cavity until the neighboring endocardial surface becomes active. Even after this the hole made by the electrode communicates with the cavity, and apparently acts as a window which cannot be closed by the polarized zone, which, according to our hypothesis, represents muscle undergoing activation. Since the point of the electrode lies opposite this window, its potential tends to follow that of nearby points inside the ventricle. When the electrode is pushed deeper, the window is farther from its point and therefore less effective.

A pure monophasic response showing no notches on its descending limb is rarely obtained from the mammalian heart except from epicardial regions where the curve obtained with a soft electrode is of the type that begins with a deep downward movement and displays an intrinsic deflection which does not rise far above the zero level. From such regions, however, pure monophasic responses are obtained without special difficulty (Fig. 5 *D*). They often show a slight thickening on the descending limb at the point where the intrinsic deflection formerly began. When the epicardial surface is injured by a stab-electrode at a point where the intrinsic deflection occurs late in the QRS interval, the excitation wave reaches the injured muscle at a time when the negative potential of the ventricular cavity is rapidly diminishing. Since the electromotive force across the ventricular wall must then have reached its maximum value, it must be constant or decreasing. If it is constant or if it is decreasing less rapidly than the negative potential of the ventricular cavity, the curve obtained continues to descend and shows no upstroke at the point where the intrinsic deflection is due.

SUMMARY

When the exploring electrode is placed in the left ventricular cavity of the dog's heart, the QRS group of the curve obtained is represented by a single deflection. The direction of this deflection is upward, indicating that the potential of this cavity is negative throughout the QRS interval. When this electrode is placed in the right ventricular cavity, the curve obtained is similar but may show a small preliminary dip preceding the main upstroke.

When the exploring electrode is placed on the epicardial surface, its potential is conspicuously different from that of the nearest portion of the ventricular cavity only during the period when the excitation wave is spreading outward through the subjacent ventricular wall. Before

the endocardial surface becomes active and after the epicardial surface has been fully activated, there is no electromotive force across the ventricular wall, and a lead from the epicardial surface is, in effect, a lead from the ventricular cavity.

The occurrence in an epicardial lead of an upward deflection which precedes the main downstroke is therefore attributed to late activation of the endocardial surface. The main downstroke is due to electric forces produced by the progress of the excitatory process outward through that portion of the ventricular wall lying between the exploring electrode and the ventricular cavity. The intrinsic deflection marks the arrival of the excitation wave beneath the exploring electrode, and hence the extinction of the electromotive force across the subjacent ventricular wall. The sudden upstroke which constitutes this deflection occurs as this electrode assumes the potential of the ventricular cavity.

The same principles may be applied to the interpretation of the curves obtained by placing the exploring electrode upon a portion of the ventricular surface of the dog's heart that has been injured. Pure monophasic curves may be obtained by means of such leads if the region injured is one where the intrinsic deflection occurs late and does not rise far above the zero level.

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FACTORS CONCERNED IN CARDIAC HYPERTROPHY

A STUDY MADE AT NECROPSY OF SEVENTY-NINE CASES OF RHEUMATIC HEART DISEASE*

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THE problems of cardiac hypertrophy have been the basis of numerous investigations as recorded in the older as well as in the more recent medical literature. As early as 1877, Cohnheim experimentally produced aortic insufficiency in dogs, in order to study the effect of this lesion on the heart. His method, unfortunately, permitted only very short periods of observation, so that his experimental conditions were in no way comparable to the condition usually observed in man. A year later Rosenbach, a student of Cohnheim, carried out experiments on rabbits, producing aortic insufficiency in some and mitral insufficiency in others, demonstrating the occurrence of cardiac dilatation and hypertrophy. His experiments covered a longer period, and the conditions produced were more comparable to the chronic lesions seen in man.

Müller, in 1883, demonstrated similar experimental results by comparing the weight of the heart to that of the body. He also studied the auricular and ventricular weights differentially by separation, but his technique has been shown to be inaccurate in the light of more recent work.¹⁷

Tangl, in 1889, produced chronic aortic insufficiency experimentally which resulted in cardiac hypertrophy, and concluded that the degree of hypertrophy depended on the time that the lesion which caused regurgitation had existed, and on its degree, and also that an increase in size of the individual muscle fibers occurred. Numerous references, other than those mentioned, may be found in the literature.

It is interesting and appropriate to review some of the hypotheses that have been advanced regarding the causes of cardiac hypertrophy: (1) Since the early part of the nineteenth century,^{5, 6, 25} increased work of the heart has been considered predominantly as the most important influence in the production of cardiac hypertrophy. (2) Possible increase in coronary blood flow as demanded by the increase in muscle mass has been suggested as a contributory influence.^{19, 24} (3) The existence of inflammatory lesions of the myocardium was considered capable of producing cardiac hypertrophy.^{1, 21} (4) An increase in in-

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terstitial myocardial tissue was believed to be a factor.^{7, 16} (5) Prolongation of the midsystolic period and its consequent prolonged hyperemia and increased local nutrition were advanced as a cause.¹⁵ (6) When the heart is subjected to overstrain, as occurs if a valvular lesion is present, the heart dilates, and in order to reestablish normal function, it must increase its force. The stimulus for this seems to lie in the residual blood in the ventricle, which acts as an increased load and tends to increase both the irritability and the force of contraction and to bring about an increase in tonicity.^{9, 12} (7) More recently, Herrmann has stressed the importance of considering not one influence but a combination of influences in the production of cardiac hypertrophy.

The present study was undertaken to determine, if possible, the major factors and their relative importance in the development of cardiac hypertrophy in man.

MATERIAL

The material which formed the basis for this study comprised seventy-nine cases of rheumatic heart disease in which careful necropsy had been conducted. The cases were carefully selected, so that all the required data were available in every instance. The requirement for inclusion demanded an accurate record of the time of the initial illness with rheumatic fever, the patient's age, sex, body weight, and height, with special data regarding the departure of each from his average normal weight during health; also were required the weight of the heart, accurate description of the cardiac lesions, including associated pathological changes, the cause of death, and records of blood pressure. Patients who had hypertension or who presented evidence suggesting previous hypertension, were not included.

METHOD OF STUDY

The heart was removed from the body in the usual manner, opened and washed before weighing.

In order to permit comparative analysis the cases were grouped according to type of valvular lesion. The valvular defect, whether it was stenotic or allowed regurgitation, or both, was graded numerically on the basis of 0 (no defect) to 4 (extreme defect) for clearness and brevity. The predominant defect was always considered first, presuming its greater influence on cardiac hypertrophy. When the defect was limited to one valve and was of one type only, it was so considered; and when defects involved more than one valve, they were grouped as such. In the case of mitral endocarditis, the defects were uniformly of the stenotic type and of the type that allowed of regurgitation, the stenotic element universally predominating.

NORMAL CARDIAC WEIGHTS

In a study predominantly dealing with cardiac weights it is necessary clearly to expound the normal values utilized. The figures for normal cardiac weights are those established by one of us (Smith) in 1928, in a carefully conducted study of 1,000 normal hearts. These figures showed that the average weight of the heart of the adult males was 294 gm. (165 to 320 gm.), and that the average weight of the heart of adult females was 250 gm. (135 to 325 gm.). The data obtained in the

study made in 1928 demonstrated a definite correlation between the weight of the heart and the weight of the body, the ratios in adults of average weight were 0.43 per cent for males and 0.40 per cent for females. Among thin persons the ratio is slightly higher, whereas among obese persons it is slightly lower. These variations in individual habitus are important, and must always be considered in the computation of cardiac weights.

The same former study²⁰ also showed that the weight of the heart can be calculated from the weight of the body, with an error varying from 8 to 10 per cent. The weight of the body in pounds is multiplied by the coefficient 1.9 for males of average weight, by 1.8 for females of average weight, by 1.6 for obese males, by 1.5 for obese females and by 2.1 for thin persons. These coefficients have been employed in this study.

It was also shown²⁰ that the weight of the heart does not increase with age, irrespective of the weight of the body. Previous data emphasizing this relationship are fallacious, probably because of the inclusion of hearts of elderly subjects who had had hypertension.

RESULTS.

In this material there were forty-two males and thirty-seven females. The average age of the patients was forty and eight-tenths years, the youngest patient was aged eleven years, and the oldest patient was aged sixty-nine years. Nine children are included in this material, and it must be emphasized here that the standards of cardiac weight of children are uncertain, and that the computations in this study with reference to children are probably associated with a greater error than those pertaining to adults.

TABLE I
CARDIAC HYPERTROPHY GROUPED ACCORDING TO VALVULAR DEFECTS
(SEVENTY-NINE CASES)

VALVULAR LESIONS	CASES	MALES	FEMALES	AVERAGES								
				AGE, YEARS	AGE AT ONSET OF RHEUMATIC FEVER, YEARS	INTERVAL FROM FIRST ATTACK OF RHEUMATIC FEVER TO DEATH, YEARS	ACTUAL HEART WEIGHT, GM.	INCREASE IN HEART WEIGHT OVER CALCULATED NORMAL, GM.	PERCENTAGE INCREASE OVER CALCULATED NORMAL	BODY WEIGHT, KG.	HEIGHT, CM.	RATIO OF HEART WEIGHT TO BODY WEIGHT
Aortic stenosis	9	8	1	48.6	17.4	31.2	686	387	51	72.6	173	0.96
Aortic insufficiency	10	7	3	40.9	17.6	23.3	574	290	47	76.3*	172*	0.82*
Multiple valvular lesions	20	12	8	38.7	18.5	20.2	524	281	50	65.2*	169*	0.86*
Mitral stenosis and insufficiency	35	13	22	39.8	17.9	21.9	469	222	46	62.4*	165*	0.76*
Mitral insufficiency	5	2	3	42.4	21.2	21.2	314	77	25	62.9*	164*	0.52*

*Children excluded in computations.

In order to permit comparative study the cases were grouped as is shown in Table I. Our first analysis concerns the average values derived in the subdivision of the cases into the foregoing groups.

The greatest cardiac weight occurred in the cases in the first group (aortic stenosis) in which the average weight was 686 gm. In order of cardiac weight, the other groups presented the following average values: aortic insufficiency, 574 gm.; multiple valvular lesions, 524 gm.; mitral stenosis and insufficiency, 469 gm.; and pure mitral insufficiency, 314 gm. The heart-weight body-weight ratios were increased 25 to 131 per cent over normal (male and female average normal 0.415 per cent) (Table I).

No definite correlation was evident between cardiac weight on the one hand and, on the other, the interval from the first attack of rheumatic fever to death. However, the longest interval appeared in the cases of aortic stenosis in which occurred the greatest average age at death. The intervals in the other groups were so closely approximated as to be insignificant.

This order of cardiac weights conforms with clinical impressions, and is in agreement with Cabot's figures, which included 1,230 post-mortem examinations.

Aortic Stenosis.—There were nine cases of aortic stenosis in which all the requirements for inclusion in this study were present. Eight of the patients were males and one was a female. The average age was forty-eight and six-tenths years; the youngest patient was thirty-one years of age, and the oldest sixty-six years. Death occurred from heart failure in six cases; in all but one case, that of sudden death, the syndrome of congestive heart failure was present. Death occurred as the result of acute bacterial endocarditis (*B. influenzae*) in one case, from pyelonephritis in one, and from pneumonia in another.

It is necessary to emphasize the fact that studies of weight in the presence of congestive heart failure include a variable error, differing considerably with the individual patient and depending on the amount of edema fluid retained. This variable, which obviously cannot be determined, may materially influence the weight of the body. Congestive heart failure occurred in 58 per cent of the entire series of seventy-nine cases.

The data in Table II are arranged according to the degree of aortic stenosis (Grade 0 to 4); Grade 4 indicates almost complete closure of the aortic orifice, whereas Grade 1 denotes slight but actual narrowing in the diameter of the orifice. A definite correlation between the degree of stenosis and the average cardiac weights is evident. The correlation between the average cardiac weights, on the one hand, and, on the other, the average intervals from the first attack of rheumatic fever to death is suggestive but not definite. Only one attack of rheu-

matie fever occurred among the patients of this group. The other data pertaining to body habitus, individual cardiac weights and so forth, are expressed in Table II.

TABLE II
CARDIAC HYPERTROPHY IN PRESENCE OF AORTIC STENOSIS (NINE CASES)

CASE	AGE, YEARS, AND SEX	BODY WEIGHT, KG.	HEIGHT, CM.	RATIO OF HEART WEIGHT TO BODY WEIGHT	CAUSE OF DEATH	STENOSIS, GRADE	ACTUAL HEART WEIGHT, GM.	INCREASE IN HEART WEIGHT OVER CALCULATED NORMAL, GM.	PERCENTAGE INCREASE OVER CALCULATED NORMAL	INTERVAL FROM RHEUMATIC FEVER TO DEATH, YEARS
1	40 M	86.3	188	1.36	Heart failure*	4	1017	656	65	28
2	62 M	72.7	184	1.35	Heart failure*	4	980	676	69	49
Averages	51	79.5	186	1.35			999	666	67	39
3	51 M	77.2	171	0.99	Heart failure*	3	770	447	58	38
4	50 M	58.6	154	1.12	Acute bacterial endocarditis	3	760	515	68	44
5	48 M	81.8	173	0.87	Heart failure*	3	717	369	51	20
6	31 F	59.0	162	0.97	Heart failure	3	573	339	59	18
Averages	45	69.2	165	0.99			705	423	59	30
7	40 M	70.4	172	0.97	Heart failure*	2	685	390	57	10
8	66 M	78.1	172	0.48	Pyelonephritis	2	356	46	13	36
Averages	53	74.2	172	0.73			521	218	35	23
9	50 M	65.0	183	0.49	Pneumonia	1	320	49	15	38

*Congestive heart failure.

Holman and Beck produced experimental aortic stenosis in dogs by constricting the aorta with tape. Three such experiments are reported, but unfortunately the terminal cardiac weight of only one animal is mentioned. The dog weighed 20 kg.; and after the lapse of six months the heart weighed 165 gm. and the heart-weight body-weight ratio was 1.21 per cent. The normal ratio for dogs is recorded as 0.72 per cent by Joseph and 0.798 per cent by Herrmann, an average of 0.76 per cent. This represents an increase in 37 per cent over the normal average heart-weight body-weight ratio. The aorta was constricted to half its normal diameter.

Eyster, Meek and Hodges produced experimental aortic stenosis in nineteen dogs, and studied the size of the heart by serial roentgenographic silhouettes, but failed to record terminal cardiac weights. The average increase in silhouette for the entire series was 10.5 per cent of the original area. The initial increase in shadow is interpreted by these workers to indicate dilatation from which the heart may entirely or partially recover, whereas subsequent enlargement, developing slowly, probably indicates hypertrophy.

Aortic Insufficiency.—This group comprised ten cases in which seven were males and three females. The average age was forty and nine-tenths years, seven and seven-tenths years less than that of patients

TABLE III

CARDIAC HYPERTROPHY IN PRESENCE OF AORTIC INSUFFICIENCY (TEN CASES)

CASE	AGE, YEARS, AND SEX	BODY WEIGHT, KG.	HEIGHT, CM.	RATIO OF HEART WEIGHT TO BODY WEIGHT	CAUSE OF DEATH	INSUFFICIENCY, GRADE	ACTUAL HEART WEIGHT, GM.	INCREASE IN HEART WEIGHT OVER CALCULATED NORMAL, GM.	PERCENTAGE INCREASE OVER CALCULATED NORMAL	INTERVAL FROM RHEUMATIC FEVER TO DEATH, YEARS
1	30 M	81.8	175	1.16	Heart failure*	3	950	608	64	10
2	62 M	80.9	171	1.11	Heart failure*	3	900	562	62	29
3	30 M	113.6	172	0.72	Heart failure†	3	826	426	52	13
Averages	41	92.1	173	1.00			892	532	59	17
4	21 F	50.9	165	1.21	Pneumonia	2	615	413	67	21
5	58 F	83.1	166	0.66	Strangulated hernia†	2	550	257	46	28
6	67 M	90.9	186	0.49	Intestinal hemorrhage	2	444	64	14	51
Averages	49	74.9	172	0.79			536	245	42	33
7	12 F	40.9	147	0.92	Heart failure*	1	376	214	57	7
8	13 M	33.8	150	1.00	Heart failure*	1	340	195	57	1
9	37 M	59.0	168	0.57	Subacute bacterial endocarditis	1	338	91	27	28
10	63 M	50.0	169	0.60	Inanition‡	1	300	69	23	45
Averages	31	55.0§	159§	0.77§			339	142	41	20

* Congestive heart failure.

† Obesity.

‡ Emaciation.

§ Children excluded in body weight and height averages.

with aortic stenosis. The youngest patient was twelve years of age and the oldest was sixty-seven years of age. Five patients died of congestive heart failure, one patient died of subacute bacterial endocarditis (*Streptococcus viridans*); whereas the remainder of the patients died from diseases unrelated to the heart (Table III).

Two patients were obese and one was emaciated, which facts were considered in the calculation of the increased weight of the heart over the normal for the given person.

The data in Table III are arranged according to the degree of aortic insufficiency (Grade 0 to 4). Again, a clear-cut correlation between the degree of lesion and the average weight of the hearts occurred. No correlation appeared between weights of the hearts, on the one hand, and, on the other, the individual and average intervals from the first episode of rheumatic fever to death. Only one attack of rheumatic fever occurred among these patients. Detailed data dealing with cardiac weight and body habitus may be noted in Table III.

We wish to call attention to Case 8 (Table III) of this group. The patient was a boy, aged thirteen years, who died of congestive heart failure one year following his first attack of rheumatic fever. The heart weighed 57 per cent more than the calculated normal cardiac weight for this boy's habitus. This case and three similar cases of patients who survived for a short time following rheumatic fever with marked cardiac hypertrophy are reported in the succeeding groups and will be considered more fully later in this paper.

It is of interest to compare these data to similar data dealing with experimental aortic insufficiency of dogs. Bazett and Sands, in their experiments on dogs, demonstrated cardiac hypertrophy, particularly of the left ventricle. They reported the results of nine experiments, the dogs surviving from two days to ten months. The heart-weight body-weight ratios of six dogs were definitely greater than the stated normal values.^{11, 14} They ranged from 0.81 to 0.91 per cent; the average was 0.87 per cent. This is greater than the average (0.82 per cent) found in our cases. The terminal weights of the dogs' hearts ranged from 91 to 177 gm.

The experimental data on aortic insufficiency were also brought out in studies by Eyster, Meek and Hodges.

Multiple Valvular Lesions.—Twenty patients had multiple valvular lesions, and the details regarding the type of lesion and the valves involved may be noted in Table IV. There were twelve males and eight females. The average age of the group was thirty-eight and seven-tenths years; the youngest patient was aged eleven years, and the oldest sixty-nine years. Twelve patients died of congestive heart failure, three of subacute bacterial endocarditis (*Streptococcus viridans*), one of coronary embolism, and the remainder from causes unrelated to the heart.

As in the previous groups, a definite correlation between the degree of lesion and the average cardiac weight occurred. Because the lesions were multiple and varied in this group, the predominant defect is considered primarily. A correlation between the average weights of the hearts, on the one hand, and, on the other, the interval from the first attack of rheumatic fever to death in these cases was evident. However, in view of the findings in the other groups, this relationship may be casual. Two patients were emaciated and one was obese, and the proper coefficients were utilized in the computations of cardiac weight.

It is interesting that multiple lesions apparently do not exert as great a mechanical effect as certain isolated lesions.

Mitral Stenosis and Insufficiency.—This group included thirty-five patients. There were thirteen males and twenty-two females. The average age for the group was thirty-nine and eight-tenths years; the youngest patient was aged eleven years, and the oldest sixty-five years. Twenty-three patients had died of congestive heart failure, five of subacute bacterial endocarditis (*Streptococcus viridans*), and the remainder from causes unrelated to the heart.

A correlation between the severity of the lesion and the average cardiac weights is again evident if the case in which the lesion was graded 4 is excluded. As this grade is represented by only one case, it is reasonable to presume that a greater number of cases would bring the average cardiac weight above that in Grade 3. The stenotic element predominated over that of insufficiency in all cases, and therefore formed the basis for grading.

Five patients in this group were the only persons in the entire series to suffer more than one attack of rheumatic fever. Four patients had two attacks; one patient had six attacks. One patient was obese, and proper recognition of this fact was made in our computations (Table V).

Mitral Insufficiency.—There were only five cases (6 per cent) of pure mitral insufficiency. It is a recognized fact that pure mitral insufficiency without stenosis is rare, and we believe that our cases thus tabulated are bona fide examples of this lesion. In these cases there were two males and three females. The average age was forty-two and four-tenths years; the youngest patient was aged thirteen years, and the oldest sixty-one years. It is interesting and significant to note that only one patient died of heart disease (Table VI).

A correlation between the degree of lesion and the average weight of the heart likewise appears to prevail in this small group of cases. No correlation between the cardiac weight, on the one hand, and, on the other, the interval from the first attack of rheumatic fever to death is evident in the individual cases, although the averages appear to show a trend.

TABLE IV
CARDIAC HYPERTROPHY IN PRESENCE OF MULTIPLE VALVULAR LESIONS (TWENTY CASES)

CASE	AGE, YEARS, AND SEX	BODY WEIGHT, KG.	HEIGHT, CM.	RATIO OF HEART WEIGHT TO BODY WEIGHT	CAUSE OF DEATH	DOM- INANT VALVU- LAR LESION, GRADE	TYPES AND GRADES OF VALVULAR LESIONS	ACTUAL HEART WEIGHT, GM.	INCREASE IN HEART WEIGHT OVER CAL- CULATED NORMAL, GM.	PERCENT- AGE INCREASE OVER CAL- CULATED NORMAL	INTERVAL FROM RHEU- MATIC FEVER TO DEATH, YEARS
1	46 M	68.1	174	0.96	Heart failure*	4	Mitral stenosis 4, aortic insuf- ficiency 2, and stenosis	658	373	57	36
2	58 M	70.0	172	1.37	Heart failure*	3	Aortic stenosis 3, mitral sten- osis 2	960	667	68	44
3	35 M	70.6	179	1.13	Subacute bacterial endocarditis	3	Aortic insufficiency 3, mitral stenosis 2	800	504	63	28
4	53 M	72.7	170	1.01	Heart failure*	3	Aortic stenosis 3, mitral sten- osis 2, mitral insufficiency 2	738	434	59	21
5	34 M	59.0	172	1.06	Heart failure*	3	Mitral stenosis 3, aortic sten- osis 2, tricuspid stenosis 2	630	383	61	13
6	13 F	31.1	154	2.24	Heart failure*	3	Aortic insufficiency 3, mitral stenosis 1	595	472	79	1.5
7	43 M	65.0	165	0.85	Heart failure*	3	Aortic stenosis 3, mitral sten- osis 2	552	280	51	15
8	68 M	59.0	177	0.91	Heart failure*	3	Aortic stenosis 3, mitral sten- osis 3, mitral insufficiency 1	542	295	54	54
9	47 M	75.0	168	0.70	Peritonitis	3	Mitral stenosis 3, aortic insuf- ficiency 3	525	211	40	10
10	12 F	36.1	149	1.42	Heart failure*	3	Mitral stenosis 3, aortic insuf- ficiency 1	517	374	72	4
11	36 F	47.2	157	0.96	Coronary embolism	3	Mitral stenosis 3, aortic sten- osis 2	452	265	59	6
12	37 M	75.0	165	0.56	General paresis	3	Mitral stenosis 3, tricuspid sten- osis 2	423	110	26	12
Averages	40	65.9†	169†	1.11†				612	363	57	19

TABLE IV—CONT'D

CASE	AGE, YEARS AND SEX	BODY WEIGHT, KG.	HEIGHT, CM.	RATIO OF HEART WEIGHT TO BODY WEIGHT	CAUSE OF DEATH	DOM- INANT VALVU- LAR LESION, GRADE	TYPES AND GRADES OF VALVULAR LESIONS	ACTUAL HEART WEIGHT, GM.	INCREASE IN HEART WEIGHT OVER CAL- CULATED NORMAL, GM.	PERCENT- AGE INCREASE OVER CALCU- LATED NORMAL,	INTERVAL FROM RHEU- MATIC FEVER TO DEATH, YEARS
13	57 F	63.6	150	0.86	Heart failure*	2	Mitral stenosis 2, aortic insuf- ficiency 2	547	295	54	15
14	69 M	58.6	177	0.80	Heart failure	2	Aortic stenosis 2, mitral sten- osis 1, mitral insufficiency 2	471	226	48	49
15	17 M	49.5	170	0.87	Subacute bacterial endocarditis†	2	Mitral stenosis 2, mitral insuf- ficiency 1, aortic insufficiency 2	435	206	47	2
16	44 F	86.8	166	0.49	Heart failure‡	2	Mitral stenosis 2, aortic insuf- ficiency 2	433	32	7	24
17	50 F	63.6	174	0.64	Poisoning	2	Mitral stenosis 2, aortic insuf- ficiency 1	407	155	38	8
18	31 F	59.5	165	0.63	Subacute bacterial endocarditis	2	Mitral stenosis 2, aortic insuf- ficiency 1	380	144	38	24
19	13 M	50.0	137	0.60	Heart failure*	2	Mitral insufficiency 2, aortic stenosis 1	300	91	30	13
20	11 F	27.2	142	0.80	Chorea‡	2	Aortic insufficiency 2, mitral in- sufficiency 2	220	94	43	1 mo.
Averages	37	63.6†	167‡	0.71†				399	155	38	17

*Congestive heart failure.

†Children excluded in body weight and height averages.

‡Emaciation.

§Obesity.

TABLE V
CARDIAC HYPERTROPHY IN PRESENCE OF MITRAL STENOSIS AND INSUFFICIENCY (THIRTY-FIVE CASES)

CASE	AGE, YEARS, AND SEX	BODY WEIGHT, KG.	HEIGHT, CM.	RATIO OF HEART WEIGHT TO BODY WEIGHT	CAUSE OF DEATH	STENOSIS, GRADE	ACTUAL HEART WEIGHT, GM.	INCREASE IN HEART WEIGHT OVER CALCULATED NORMAL, GM.	PERCENTAGE INCREASE OVER CALCULATED NORMAL	INTERVAL FROM RHEUMATIC FEVER TO DEATH, YEARS
1	43 M	63.6	171	0.62	Heart failure*	4	413	147	36	28
2	52 F	60.9	158	1.20	Heart failure*	3	730	489	67	48
3	33 M	65.9	181	1.07	Heart failure*	3	707	431	61	16
4	48 F	45.9	165	1.45	Heart failure*	3	665	483	73	26
5	21 M	75.0	175	0.86	Heart failure*	3	644	330	51	8
6	65 M	84.0	171	0.75	Heart failure*	3	630	278	44	50
7	44 M	58.6	177	1.04	Heart failure*	3	610	365	60	4
8	38 M	58.1	179	0.99	Heart failure*	3	585	342	58	26
9	53 F	54.5	156	1.02	Heart failure*	3	557	341	61	41
10	45 F	59.0	165	0.93	Heart failure*	3	548	314	57	21
11	21 M	56.8	179	0.90	Subacute bacterial endocarditis	3	514	276	54	7
12	45 F	90.9	172	0.53	Heart failure*†	3	489	169	35	16
13	36 F	75.0	165	0.62	Heart failure*	3	465	168	36	15
14	43 F	51.8	163	0.89	Heart failure*	3	465	260	56	33
15	34 M	54.5	165	0.78	Heart failure*	3	429	201	47	9
16	48 F	46.8	159	0.90	Cerebral embolism	3	425	240	56	36
17	40 F	54.5	166	0.75	Heart failure*	3	410	194	47	14
18	37 F	54.0	162	0.62	Heart failure*	3	340	126	37	27
Averages	41	61.5	166	0.90			542	294	53	23

* Congestive heart failure.

† Obesity.

‡ Children excluded in body weight and height averages.

TABLE V—Cont'd

CASE	AGE, YEARS, AND SEX	BODY WEIGHT, KG.	HEIGHT, CM.	RATIO OF HEART WEIGHT TO BODY WEIGHT	CAUSE OF DEATH	STENOSIS, GRADE	ACTUAL HEART WEIGHT, Gm.	INCREASE IN HEART WEIGHT OVER CALCULATED NORMAL, Gm.	PERCENTAGE INCREASE OVER CALCULATED NORMAL	INTERVAL FROM RHEUMATIC FEVER TO DEATH, YEARS
19	50 M	95.4	174	0.77	Uremia	2	712	313	44	29
20	16 F	47.7	165	1.05	Subacute bacterial endocarditis	2	505	316	62	11
21	40 M	84.0	169	0.57	Subacute bacterial endocarditis	2	485	133	27	22
22	37 M	79.5	173	0.59	Heart failure*	2	470	137	29	4
23	37 F	48.1	164	0.93	Heart failure*	2	450	259	58	29
24	55 F	81.8	171	0.54	Brain tumor	2	444	120	27	37
25	23 F	44.5	157	0.91	Subacute bacterial endocarditis	2	405	229	57	13
26	61 F	79.5	172	0.50	Diabetic gangrene	2	397	82	21	31
27	23 F	45.4	160	0.90	Subacute bacterial endocarditis	2	390	210	54	10
28	40 M	56.8	178	0.61	Heart failure*	2	350	112	32	19
29	53 F	68.1	165	0.51	Heart failure*	2	349	79	23	42
30	23 F	61.3	163	0.55	Heart failure*	2	337	94	28	12
31	42 F	45.4	162	0.70	Pneumonia	2	320	140	44	24
32	48 F	60.4	158	0.52	Exophthalmic goiter	2	315	76	24	32
33	29 F	45.2	155	0.66	Heart failure*	2	300	105	35	17
34	11 M	32.7	140	0.90	Heart failure*	2	294	157	53	6
Averages	37	63.6†	170†	0.70†			408	160	40	21
35	62 F	54.5	158	0.52	Carcinoma of common bile duct	1	283	67	24	9

TABLE VI
CARDIAC HYPERTROPHY IN PRESENCE OF MITRAL INSUFFICIENCY (FIVE CASES)

CASE	AGE, YEARS, AND SEX	BODY WEIGHT, KG.	HEIGHT, CM.	RATIO OF HEART WEIGHT TO BODY WEIGHT	CAUSE OF DEATH	INSUFFI- CIENCY, GRADE	ACTUAL HEART WEIGHT, GM.	INCREASE IN HEART WEIGHT OVER CALCULATED NORMAL, GM.	PERCENTAGE INCREASE OVER CALCULATED NORMAL	INTERVAL FROM RHEUMATIC FEVER TO DEATH, YEARS
1	28 M	78.6	167	0.54	Pneumonia	2	396	67	17	20
2	60 F	73.6	155	0.47	Carcinoma of rectum	2	351	59	17	26
3	61 F	54.5	160	0.54	Cachexia of carcinoma	2	297	81	27	49
4	13* F	36.3	149	0.81	Heart failure*	2	295	151	51	4 months
Averages	41	68.9†	161†	0.59†			335	90	28	24
5	50 M	45.0	175	0.51	Ulcerative colitis‡	1	232	25	11	12

* Congestive heart failure.

† Children excluded in body weight and height averages.

‡ Functio laesa.

COMMENT

In a recent investigation, Levine and Carr divided and weighed a series of hearts of human beings according to the experimental method of Herrmann.¹⁰ Fractional weights were determined in fifteen cases of rheumatic heart disease, including five cases of mitral stenosis and insufficiency, three cases of aortic stenosis and insufficiency, five cases of mitral and aortic stenosis and insufficiency, one case of mitral, aortic, and tricuspid stenosis and insufficiency, and one case of thrombo-endocarditis of the mitral valve. The conclusions pertinent to this study are that in rheumatic defects of the mitral valve alone the increase in cardiac weight is the result of an increase in the weight of the right ventricle and the auricles. In large hearts associated with aortic insufficiency, rheumatic or syphilitic, hypertrophy of the whole heart occurs, but the greatest increase is in the left ventricle. Levine and Carr expressed the belief that mechanical factors are not entirely responsible for the production of cardiac hypertrophy.

We shall attempt to apply the analysis of our data to the various hypotheses advanced regarding the production of cardiac hypertrophy.

The hypothesis that increased cardiac work causes hypertrophy finds unmistakable confirmation in this study, as almost without exception the average weight of the hearts paralleled the degree of valvular deformity. The work demanded of the heart appears to be primarily concerned with the magnitude of the mechanical barrier. In considering increased work, however, the interval of time during which the heart is subjected to increased work cannot be disregarded; and although it undoubtedly plays an important part in many cases, the mechanical factor may exert its influence overwhelmingly, so that the time element apparently becomes submerged.

Our study does not deal with the coronary circulation, so that we do not have data regarding coronary blood flow and cardiac hypertrophy. We know of no proof to the effect that an increase in muscle mass provokes an increase in coronary blood flow, thus furthering cardiac hypertrophy. In fact, the opposite conclusion is not improbable, that in greatly hypertrophied hearts the normal coronary circulation becomes relatively insufficient, since its work may be doubled or even trebled, as the case may be.

The question of the relationship of inflammatory lesions of the myocardium to cardiac hypertrophy is one of considerable interest. In this connection it is important to consider the cases of the four children briefly mentioned earlier in this paper who survived for short periods following their first rheumatic infection.

REPORT OF CASES

CASE 1.—(Case 8, Table III.) A boy, aged thirteen years, died of congestive heart failure one year following his first attack of rheumatic fever. Only a slight degree of aortic insufficiency (Grade 1) was found at necropsy, but the heart weighed

340 gm., an increase of 195 gm. (57 per cent) over the calculated normal. Neither the degree of the mechanical lesion nor the duration of the lesion seemed capable of producing cardiac hypertrophy of this magnitude. This boy had had only one attack of rheumatic fever.

CASE 2.—(Case 6, Table IV.) A girl, aged thirteen years, died of congestive heart failure one and a half years following the first episode of rheumatic fever. Multiple lesions were present; namely, aortic insufficiency Grade 3, and mitral stenosis Grade 1. Marked hypertrophy was found, the heart weighing 595 gm., an increase of 472 gm. (79 per cent) over the calculated normal.

CASE 3.—(Case 4, Table VI.) A girl, aged thirteen years, survived only four months after the initial and only attack of rheumatic fever and died of congestive heart failure. The only valvular defect demonstrable was mitral insufficiency Grade 2; yet the heart weighed 295 gm., an increase of 151 gm. (51 per cent) over the calculated normal.

CASE 4.—(Case 20, Table IV.) A girl, aged eleven years, was of unusual interest owing to the extremely brief survival period. She died one month after the onset of

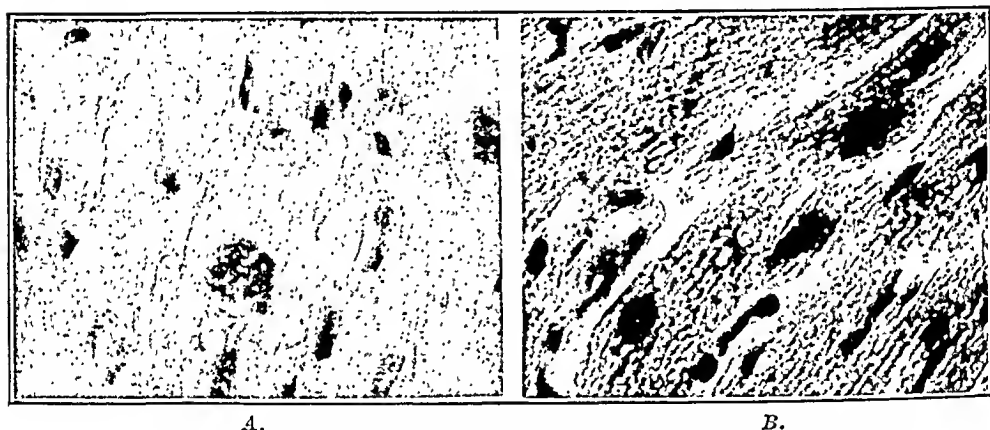


Fig. 1.—A, Section of normal heart muscle; B, section of heart muscle in Case 3 (Case 4, Table VI), marked vacuolar degeneration.

chorea. The valvular lesions demonstrated after death consisted of aortic and mitral insufficiency Grade 2. The heart weighed 220 gm., an increase of 94 gm. (43 per cent) over the calculated normal.

One of us repeatedly observed these children, and we are certain that no preexisting cardiac lesion was responsible for the cardiac hypertrophy. The cardiac injury without question occurred with the infections as stated.

Careful microscopic study of numerous sections of heart muscle of these four subjects revealed unusually marked evidences of myocarditis (Figs. 1, 2 and 3). There were extensive areas of cellular infiltration, the cells consisting chiefly of polymorphonuclear leucocytes and small lymphocytes, and certain areas revealed numerous erythrocytes. Considerable fibrin was deposited in these regions. Considerable swelling of the muscle fibers was apparent, and their striations were indistinct. There were numerous collections of cells scattered throughout the

myocardium resembling Aschoff cells. The changes described were most prominent in Cases 1 and 2, although they were well marked in the other two cases.

It appears that the marked myocarditis of these children was the chief factor contributing to the production of the cardiac hypertrophy, in view of the fact that the degree of endocarditis present and its resulting valvular deformity were considerably less than that occurring in the majority of cases. Stewart's experimental work indicated a relationship between myocarditis and cardiac hypertrophy. He produced extensive myocarditis in rabbits by intravenous injection of epinephrine, and found ensuing hypertrophy of considerable degree. The exact manner in which myocarditis produces hypertrophy is not clearly understood, but it is not improbable that it may represent a

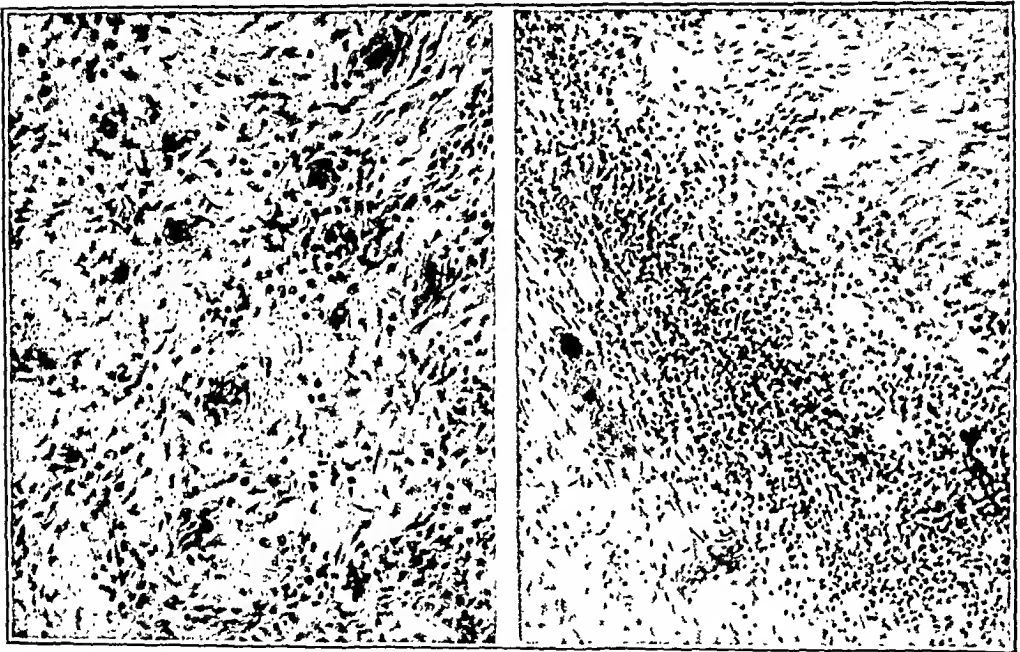


Fig. 2.

Fig. 3.

Fig. 2.—Section of heart muscle from Case 4, showing Aschoff cells.

Fig. 3.—Section of heart muscle from Case 4, showing areas of marked cellular infiltration.

compensatory effort on the part of regions of normal or relatively normal muscle. These findings strongly suggest that in some cases of severe infection the myocardium responds to the injury of hypertrophy.

Our investigation resulted in no data concerning the influence of increase in the midsystolic period on cardiac hypertrophy, nor on the influence of residual blood in the ventricle.

We concur with Herrmann in his belief that a combination of influences participates in the production of cardiac hypertrophy.

CONCLUSIONS

1. The greatest average cardiac weight occurred in cases of aortic stenosis. In order of cardiac weight other lesions occurred in the

following sequence: aortic insufficiency, multiple valvular lesions, mitral stenosis and insufficiency, and pure mitral insufficiency.

2. There was an outstanding correlation between the degree of the lesion and the average weight of the heart.

3. There was a suggestive correlation, evidenced only in some groups, between the average weight of the heart, on the one hand, and, on the other, the interval elapsing from the initial attack of rheumatic fever to death.

4. The condition of four children, who lived only for a very short time following their first illness with rheumatic fever, and chorea in one case, and three of whom had rather slight valvular defects, strongly suggests that myocardial injury by infection or its toxins in some instances permits the heart to respond by hypertrophy.

5. Although increased cardiac work imposed by the valvular defect or defects appears to be the outstanding influence in the production of cardiac hypertrophy in rheumatic heart disease, other factors appear to exert a definite but less important influence. Among them is the length of time that the heart is subjected to the lesion and actual myocardial injury in a certain group of cases.

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THE PULMONARY AND PLEURAL COMPLICATIONS OF AORTIC ANEURYSM*

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ONE of the ways in which an aneurysm of the aorta may masquerade is in the form of a chronic pulmonary or pleural infection. This is especially true of aneurysms of the descending part of the arch of the aorta and is commonly the result of compression of the trachea or bronchi with its complications. Other causes are obstruction of the pulmonary veins, direct invasion of the lung, hemorrhage into the pleural cavity, bronchoesophageal fistula, or an intercurrent tuberculosis of the pleura or lungs.

In view of the fact that these pleural and pulmonary complications may completely dominate the clinical picture, we have reviewed and analyzed the clinical and pathological features of 22 cases of aneurysm of the aorta in which the main symptoms and signs were referable to the lungs or pleura. We present here the results of this study. The cases are briefly summarized in Tables I and II.

COMMENT

General Features.—Of the 22 cases summarized in Table I, only 2 occurred in women. The patients' ages varied from twenty-eight to seventy-one years, the majority being between thirty and sixty years old. The symptoms referable to the chest varied in accordance with the position of the aneurysm and the mechanical embarrassment produced by the mass. Thus, pain, cough and expectoration, dyspnea and hemoptysis were the common symptoms. Data concerning the character of the lesions together with the type of complications produced in the lungs and bronchi are summarized in Table II. Compression of the trachea or of the bronchi, more often the left, were the commonest complications; and bronchopneumonia, lung abscesses, and bronchiectasis were the most frequent results of these lesions. The signs, therefore, depended upon the type of complication, and are discussed in more detail below. Once infection was present, fever and leucocytosis were the rule, the temperature was irregular, varying between 100° and 105° F.; the white blood cells between 6,800 and 68,000 per cubic millimeter. The duration of the pulmonary symp-

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toms and signs varied from ten days to as long as three years; in most cases, however, from a few weeks to a few months.

From the cases summarized in Table I, and others reported in the literature,¹⁻¹⁰ it is evident that a variety of pulmonary and pleural lesions may result indirectly from an aneurysm of the aorta. Indeed, as we have stated, these complications may be so prominent that they completely dominate the clinical picture. Of the 4,000 cases of aortic aneurysm collected by Boyd¹¹ the incorrect diagnoses that had been made in 130 were summarized. In about half of these cases the diagnosis was some form of pulmonary or pleural infection. Among the conditions mentioned were tuberculosis, asthma, chronic bronchitis, pleural effusion, pleural empyema, pericarditis, pleurisy, and abscess of the lung. As a matter of fact, in the cases observed by us all of these conditions occurred and, in addition, hemothorax, bronchiectasis, atelectasis, and rupture of the aneurysm into the lung. The diagnosis of aneurysm may be difficult in the presence of one of the above mentioned complications, but should be entertained in any case of obscure pulmonary or pleural infection. These various complications will be discussed in some detail.

Tracheal Compression.—This usually results from pressure on the trachea by an aneurysm of the innominate artery or of the transverse arch of the aorta. Of the cases recorded in Table I there were five cases of aneurysm of the transverse arch and two cases of aneurysm of the innominate artery causing tracheal compression. The symptoms and signs were cough, dyspnea, stridor, chronic tracheobronchitis, with signs of emphysema and bilateral bronchopneumonia. One may observe: (1) attacks of acute bronchitis with bronchopneumonia and temporary recovery; (2) chronic bronchitis followed by bronchopneumonia and death; (3) chronic bronchitis with recurrent bouts of fever, gradual failure, bronchiectasis, and death; (4) gradual suffocation due to retention of tracheal and bronchial secretions; (5) rupture of aneurysm into the trachea. An aneurysm in this location is not difficult to detect clinically and should give rise to no diagnostic difficulties. Case 4 illustrates the course of events when the trachea is compressed.

It was of considerable interest that tracheal compression was accompanied by bilateral anatomical lesions and physical signs, such as emphysema, chronic bronchitis, and bronchopneumonia. This was in striking contrast to the cases in which a main bronchus was compressed. The following case illustrates the course of events when the trachea was compressed:

CASE 4.—*A man with an aneurysm of innominate artery has symptoms and signs of tracheal compression with bilateral bronchopneumonia. Death due to rupture into trachea.*

TABLE

SUMMARY OF TWENTY-ONE CASES OF AORTIC ANEURYSM

CASE NO.	AGE SEX	SYMPTOMS	SIGNS	DURATION OF PULMONARY SIGNS
<i>Tracheal</i>				
1	55 ♂	Cough—6 mo. Dyspnea—6 mo.	Aortic insufficiency. Compression of right main bronchus. Tracheal compression. Bilateral bronchopneumonia.	6 months.
2	37 ♂	Cough—3 yr. Expectoration—1 mo.	Tracheal compression. Râles both lungs with bronchopneumonia.	3 years. Acute—1 month.
3	49 ♂	Cough and expectoration—9 wk. Dyspnea—3 wk.	Tracheal compression. Bilateral bronchitis.	6-9 weeks.
4	57 ♂	Cough—3 wk. Expectoration—2 wk. Dyspnea—5 wk.	Tracheal obstruction. Bilateral bronchopneumonia.	5 weeks.
5	60 ♂	Cough—4 mo. Expectoration.	Emphysema and chronic bronchitis. Aneurysm of transverse arch.	4 weeks when first seen.
6	46 ♂	Pain in back. Shortness of breath.	Bilateral bronchopneumonia.	Pain in left shoulder and back of neck, shortness of breath—1½ mo. Choking in throat, dysphagia—2 wk. Cough—10 days. Hemoptysis—4 days. Purulent bronchitis.
7	39 ♂	Difficulty in breathing. Cough.	Tracheal obstruction. Right radicle less than left. W. R.+ Bilateral bronchopneumonia. Neck seems distended.	2 months. Difficulty in breathing.
<i>Bronchial</i>				
8	42 ♂	Pain—2 mo. Dyspnea—7 mo. Cough and expectoration—9 mo. Loss of weight—6 mo. Dysphagia—3 mo.	Solidification of right upper lobe. Bronchopneumonia right lung. Pulsus differans.	9 months.
9	65 ♂	Cough, expectoration, loss of weight.	Limited expansion. Dullness left tip. Râles faint left axilla.	Weakness, cough—5 wk. duration. Mucopurulent sputum.
10	38 ♂	Cough and expectoration—3 wk. Pain in chest—5 days.	Aortic insufficiency. Bronchial obstruction left side. Bronchopneumonia left lower lobe.	3 weeks.

I

WITH PULMONARY AND PLEURAL COMPLICATIONS

TEMPERATURE	WHITE BLOOD CELLS THOUSANDS PER C.M.M.	PATHOLOGICAL CHANGES	REMARKS
<i>Compression</i>			
97°-103°	14.0	Aneurysm compressing right bronchus and trachea. Acute bronchitis and bronchopneumonia. Fibrinopurulent pericarditis.	.
101°-103°	16.0	Autopsy not done.	Purulent sputum.
97°-99.5°	10.3	Aneurysm compressing and eroding the trachea.	
100°-102°	14.5	Aneurysm of innominate artery. Tracheal compression. Chronic bronchitis. Rupture into trachea.	
98°-101°	34.5	Recovered.	.
98°-102°	6.1	Aneurysm of transverse aortic arch. Purulent bronchitis. Compression of trachea with opening.	
99°-101.5°	15.5	Aneurysm of innominate with obliteration of right subclavian artery. Erosion of trachea with compression. Bronchopneumonia — both lower lobes.	
<i>Compression</i>			
99°-104°	6.0-18.0	Compression of right bronchus. Abscess and bronchiectasis of right lung. Narrowing of orifice of innominate artery.	Patient had been admitted to sanatorium for tuberculosis. 50 to 100 c.c. sputum daily.
98°-101°	12.2	Aneurysm with pressure erosion of spine and left main bronchus. Bronchopneumonia. Slight bilateral hydrothorax.	.
99°-102°	9.0-11.3	Hydrothorax, right-sided. Compression of left bronchus. Bronchopneumonia left lung.	Patient had a similar attack of pulmonary disease one year before death.

TABLE

CASE NO.	AGE SEX	SYMPTOMS	SIGNS	DURATION OF PULMONARY SIGNS
11	56 ♂	Cough—1 mo. Cough and expectoration —3 wk. Fever—5 days. Dyspnea.	Compression left main bronchus.	1 month.
12	28 ♀	Dyspnea, cough and pain in chest.	Signs of fluid at left base. Coughed up blood and died.	10 weeks.
13	30 ♂	Pain—2 yr.	Stridor. Bronchial com- pression left bronchus. Bronchopneumonia left lung.	2 weeks—recovery.
14	45 ♂	Dyspnea—2 yr. Cough and expectoration —6 mo. Loss of weight. Pain.	Pneumonia left lower lobe. Compression of left upper lobe.	6 months.
15	71 ♀	Pain—5 yr. Dyspnea—2 yr.	Compression of left main bronchus.	2 years.
<i>Invasion of</i>				
16	38 ♂	Pain in right chest—10 days.	Signs of right pleural effusion.	7 weeks.
17	58 ♂	Pain in chest—2 yr. duration.	Dullness over left upper lobe.	5 days.
18	65 ♂	Pain—1 yr. Repeated hemoptyses—9 mo.	Dullness and râles over left upper lobe.	9 months.
<i>Tuber</i>				
19	52 ♂	Pain. Dyspnea.	Pleural effusion left side. Pulsus differans.	6 months.
20	45 ♂	Pain in chest and back. Cough—4 wk. Tbe. right upper lobe.	Signs of tbe. of right upper lobe.	4 weeks. Aneurysm ruptured into right lung.
21	51 ♂	Weakness, dyspnea and swelling of legs—3 wk. Bronchitis—4 yr.	Bilateral broncho- pneumonia.	Signs of bronchopneu- monia with failure —3 weeks.

I—CONT'D

TEMPERATURE	WHITE BLOOD CELLS THOUSANDS PER C.MM.	PATHOLOGICAL CHANGES	REMARKS
99°-101°	14.8	Aneurysm compressing trachea, left bronchus, left lung.	Organizing pneumonia left lower lobe. Had acute attack one month before.
98.6°	10.6	Aneurysm of descending aorta. Rupture into left bronchus. Atelectasis of left lung with pleural effusion left. Emphysema right lung. Right cavity obliterated by fibrous adhesions.	
102°-105°	10.2		Recovered from an acute attack of pneumonia. Wassermann reaction negative. X-ray signs of aneurysm.
100°-104°	18.0-27.0	Aneurysm of descending arch. Compression of left main bronchus. Bronchiectasis of left lower lobe. Compression of left upper lobe.	Mass did not pulsate on fluoroscopic examination.
98°-99°	6.0	Aneurysm of arch of aorta compressing left main bronchus. Atelectasis of left lower lobe. Rupture into bronchus.	
<i>Pleura or Lung</i>			
99°-101°	28.2	Aneurysm of descending aorta. Rupture into right pleural and pericardial cavity.	
99°-101°	15.0-21.0	Aneurysm of descending arch of aorta. Rupture into left lung and pleural cavity.	
98.6°-100°	6.0	Aneurysm invading left lung. Rupture into lung.	Anemia developed from loss of blood. Hgb. 50 per cent.
<i>culosis</i>			
99°-103°	6.0	Tuberculosis of pleura resulting from Pott's disease. Aneurysm of descending arch of aorta.	
101°	Not given	Rupture of sacular aneurysm of the transverse arch of aorta with extension post into bodies of the vertebrae and left lung. Pulmonary tbc.	
99°-101°	12.95	Aneurysm of transverse arch of aorta. General pulmonary tbc. with cavitation.	Diffuse tbc. No clinical signs of aneurysm. Cardiac insufficiency.

A man, fifty-seven years of age, complained of cough and inability to breathe comfortably of five weeks' duration. Three weeks before entering the hospital he began to have frequent attacks of coughing with profuse expectoration. Shortness of breath persisted, and there was some dull aching pain beneath the sternum. Upon examination he was dyspneic, with stridor and signs of emphysema with diffuse fine râles over both lungs. The breath sounds were distant and somewhat obscured by the râles. The cough was "brassy." There was definite pulsation in the episternal notch and in the infra- and supraclavicular fossae. There was a definite tracheal tug, and the right radial pulse was of larger volume than the left. The white blood count was 14,000 per cubic millimeter and there was no fever. Following a bout of coughing he spat up a large quantity of blood and rapidly died. The clinical diagnoses were: aneurysm of the innominate artery, compression of the trachea, tracheobronchitis, rupture of aneurysm into trachea. This was confirmed by necropsy.

This case illustrates that tracheal compression may result from an aneurysm of the innominate artery. Compression of the trachea is more common, of course, from an aneurysm of the transverse arch of the aorta.

TABLE II

SUMMARY OF PULMONARY AND PLEURAL COMPLICATIONS IN TWENTY-ONE CASES OF ANEURYSM OF THE AORTA

ANATOMICAL LESIONS	NUMBER OF CASES
<i>Tracheal Compression</i> -----	7
Bilateral bronchitis -----	4
Bilateral bronchopneumonia -----	3
<i>Bronchial Compression</i> -----	8
<i>Left Main Bronchus</i> -----	7
Bronchiectasis left lower lobe -----	1
Bronchopneumonia left lung -----	3
Hydrothorax -----	2
Organizing pneumonia left lower lobe -----	1
Collapse of left lower lobe -----	2
<i>Right Main Bronchus</i> -----	1
Abscess and bronchiectasis of right upper lobe -----	1
<i>Direct Invasion of Lung or Rupture Into Pleura</i> -----	3
Rupture into pleura -----	2
Direct invasion of lung -----	1
<i>Pulmonary and Pleural Tuberculosis</i> -----	3

Bronchial Compression.—There were eight cases (8-15) in which one of the main bronchi was compressed. In seven the left bronchus was involved, and in the other the right bronchus. In most cases of bronchial compression the aneurysm arises from the descending arch of the aorta. This was not difficult to understand when one appreciates that one of the commonest sites for aneurysms to occur is at the point where the aorta passes over and above the left main bronchus. The symptoms produced by bronchial compression were cough, expectoration, stridor, dyspnea, and attacks of suffocation. At first, when the obstruction was incomplete, there was emphysema of the left lung. Later, when secretions were retained distal to the ob-

struction, there appeared varying degrees of collapse of the lung with or without pneumonia, acute or organized, abscess or bronchiectasis. Once the infection became established, the patients had symptoms of a suppurative pulmonary lesion with fever, loss of weight, sweating, and other constitutional symptoms accompanying a chronic infection. Under these circumstances a diagnosis of tuberculosis may be made, and since both conditions may coexist, one must exclude tuberculosis before being completely satisfied with the diagnosis of "aneurysmal phthisis."

In every case in this group the pulmonary complications were on the same side as the bronchial compression. Moreover, they were more severe, as far as the local pulmonary process was concerned, than when there was tracheal obstruction. In other words, unilateral obstruction may be more complete and produce more extensive pulmonary lesions without rapid death than when there are pulmonary complications resulting from tracheal compression. On occasions, intrinsic tracheobronchial stenosis due to syphilis may cause collapse of the lobe of the lung. This may be associated with an aneurysm, as in a recent case reported by Mallory,¹² or it may be an isolated lesion, the latter being more common. Cases 15 and 14 illustrate the course of events following bronchial compression in patients with an aneurysm of the descending arch of the aorta.

CASE 15.—An elderly woman with an aneurysm of the descending arch of the aorta shows recurrent collapse of the left lung due to compression of left main bronchus; obliterative endarteritis syphilitica of left common carotid artery and partial occlusion of the innominate and left subclavian artery. Death follows rupture of aneurysm into left main bronchus.

A white woman seventy-one years of age was first seen two years before death on account of pain over the precordium. She stated that for five years she had suffered from periodic attacks of pain over the precordium and upper part of the left chest. The pain continued with rest and was not increased by exertion; it was worse when she lay on the left side. Examination at that time revealed a small woman with increased retromanubrial dullness, dullness and distant breath sounds over the left lower lung lobe. She left the hospital after several days.

Shortly after leaving the hospital she had an attack of pneumonia from which she recovered completely. Nine months before death she was readmitted to the clinic on account of pain in the chest, cough, and some shortness of breath. Upon examination it was found that she was thin and frail and had lost some weight. The positive findings were a displacement of the trachea to the left, the signs of atelectasis of the lower lobe of the left lung, and inequality of the brachial pulses, the right being less than the left. No pulsation was felt in the left carotid artery and only slight pulsation in the right. There was no lymph node enlargement and no definite tracheal tug. The heart was displaced to the left so that the apex impulse was felt in the axilla. There were no signs of aortic insufficiency. There was, however, a systolic murmur at the apex. The abdomen and extremities were negative. There was no anemia. The Kahn reaction was positive and the x-ray examination confirmed the diagnosis of atelectasis of the left lung (see Fig. 1). At this time the patient remained on the ward six weeks without any essential changes in

her physical signs—no fever, but a slight cough without expectoration. The pain became less intense and she left the hospital. Two months later she was readmitted on account of the symptoms of cystitis. The thoracic signs were the same as on the previous admission except a definite pulsation could now be seen on the left side of the chest in the second, third and fourth costal interspaces. After several weeks the signs of cystitis subsided and she left the hospital once again, to return four

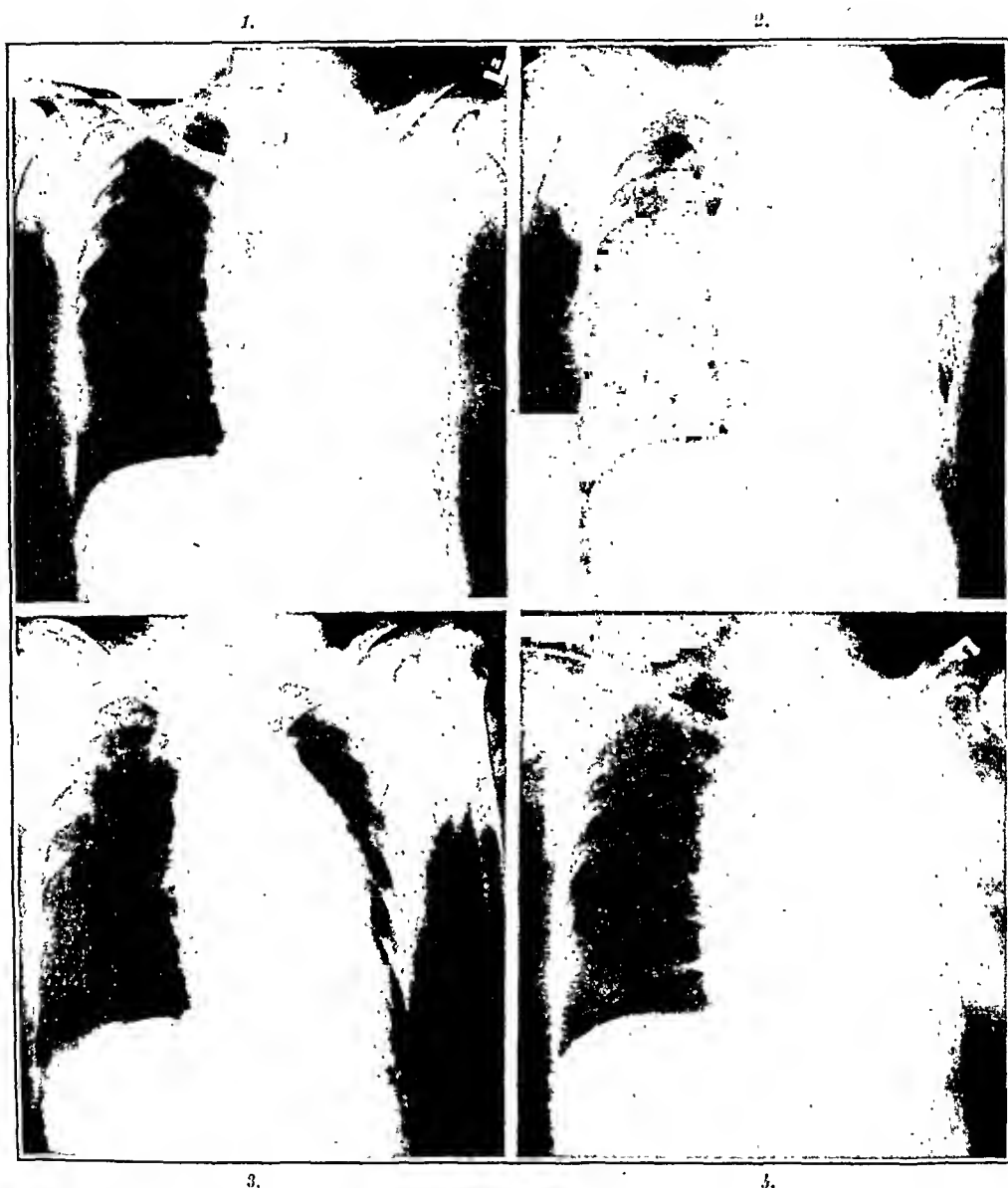


Fig. 1.—(Case 15.) Radiograms of chest taken at different intervals during the course of the illness.

(1) Nine months before death—showing collapse of lung with heart displaced to the left. Partial aeration of left upper lobe. (2) Six months before death—partial collapse of left lung. (3) One month before death—the lung has reexpanded, showing the aneurysm of the descending portion of the aortic arch. (4) One week before death—collapse of lung with signs of fluid at left lower lobe.

months later complaining of shortness of breath and a “cold in the chest.” On the first examination she showed the signs compatible with an aneurysm of the aorta, but the signs over the left lung had changed so that the breath sounds were well

heard over the lower lobe. It seemed obvious that the lung had re-expanded, and this was proved by x-ray examination. Later, following an attack of dyspnea, the signs of pulmonary collapse reappeared and were confirmed by x-ray examination. Three weeks before death she had a right-sided hemiparesis, which lasted two days. The day of death she began to cough and, after expectorating large quantities of blood, died. The clinical diagnoses were: (1) syphilitic aortitis; (2) aneurysm of aorta; (3) compression of left main bronchus; (4) atelectasis of left lung; (5) obliterative endarteritis of vessels of arch of aorta with complete occlusion of left common carotid and stenosis of the other branches; (6) rupture of aneurysm into left bronchus.

These diagnoses were confirmed by necropsy, and Fig. 2 shows the area of bronchial compression, together with the point of rupture.

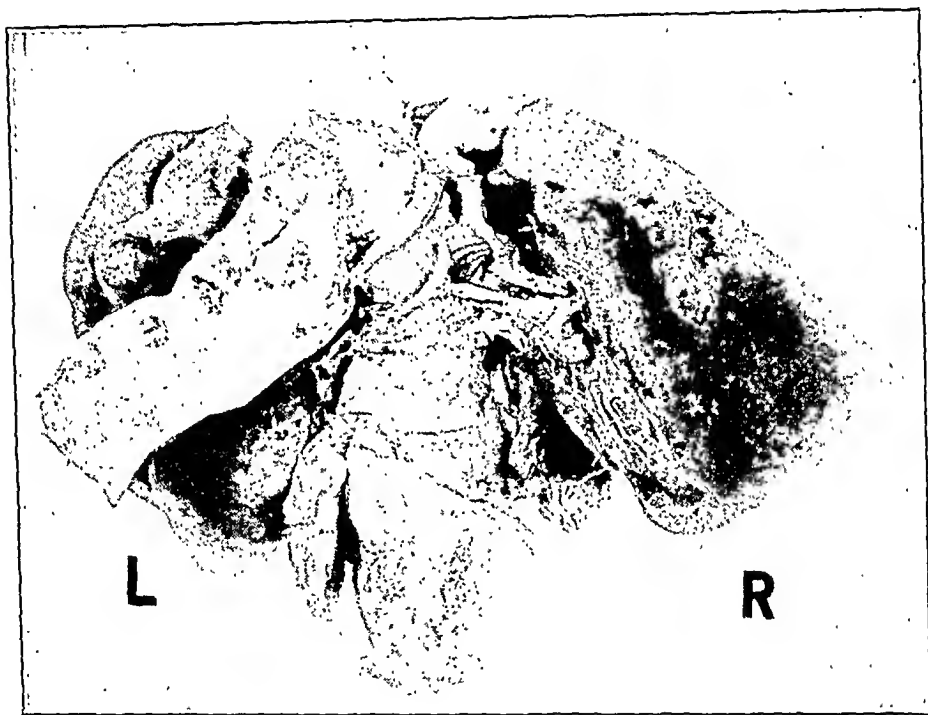


Fig. 2.—(Case 14.) Photograph showing compression and rupture of left main bronchus by aneurysm of descending arch of aorta. The left lower lobe is collapsed. The photograph was taken to show the posterior aspect of bronchi, heart and lungs.

From this case it is evident that recurrent collapse of the lung may follow bronchial compression due to aneurysm of the aorta. In other cases, an infection of a part of the lung which is supplied by the compressed bronchus is the predominating lesion as in Case 14.

CASE 14.—A man with an aneurysm of the descending arch of the aorta has fever, leucocytosis, signs of bronchial compression and bronchiectasis of the left lower lobe. Death due to infection.

An emaciated white man, forty-five years of age, complained of cough and shortness of breath on exertion, of six months' duration. For five months he had had attacks of coughing, accompanied by expectoration of mucoid material. There had been loss of weight, dizziness upon rising, pain over the precordium coming on in paroxysms unrelated to exertion and referred to the left shoulder. For six weeks his symptoms had been worse, and he had been bedridden most of this time.

Upon examination his temperature was 104° F., pulse rate 130 and respirations 27 per minute. The cough was paroxysmal in nature and the sputum was mucopurulent. The right lung was clear, the left showed signs of bronchial compression, especially over the left lower lobe where there were râles and distant breath sounds of a wheezing character. There was a tracheal tug when the trachea was displaced to the left side. The red blood cell count was 3,700,000 per cubic millimeter, the hemoglobin 65 per cent, the white blood cell count 18,300 with 76 per cent polymorphonuclear leucocytes. The Wassermann reaction was positive, and there was a mediastinal mass which did not pulsate when examined by the fluoroscope.

During the entire period of observation which lasted three weeks, there was irregular fever varying from 100° to 103° F.; the signs in the chest persisted and the patient continued to lose weight. Death resulted from infection.

From these two cases it is seen that bronchial compression may produce either collapse of the lung or a chronic infection with bronchiectasis. In either case the pulmonary symptoms and signs may predominate.

Rupture Into Pleural Cavity or Lung.—There were three cases (16-18) in which the aneurysm ruptured into the pleural cavity or lung. In one case the aneurysm invaded the left lung directly, and the outstanding feature of the case was recurrent hemoptysis. In the other two cases a hemothorax occurred, and the patient continued to live for some days or weeks before dying. A hematoma following the rupture of an aneurysm may be localized so as to simulate a malignant tumor,⁹ or it may be so large as to be confused with a hydrothorax. The latter condition occurs as a complication of an aneurysm following the collapse of the lung or compression of the azygos or pulmonary veins. The fluid in these cases has the characteristics of a transudate and is more commonly left-sided. Case 16 illustrates the course of events when an aneurysm ruptures into the right pleural cavity.

CASE 16.—A man with a right hemothorax due to an aneurysm of the ascending arch of the aorta dies as a result of hemorrhage into pericardium.

A colored man, thirty-eight years of age, complained of pain in the right side of his chest. He had been well until ten days before admission, when he noticed a dull aching pain in the right side of his chest in the posterior axillary line which was exaggerated by respiratory effort. The day before admission the pain became more severe, dyspnea and orthopnea were present, and there was an increased amount of coughing with white, frothy, blood-streaked sputum. The past history was irrelevant.

Upon examination the temperature was normal, pulse rate 100 per minute, respirations 28 and the blood pressure was 90 mm. Hg systolic and 70 mm. Hg diastolic. He was well developed, somewhat malnourished, orthopneic, and uncomfortable on account of pain and dyspnea. The pupils were normal. The trachea was deviated to the left but there was no tracheal tug. The carotid and radial pulses were equal in volume. There were signs of fluid in the right pleural cavity, the percussion note being flat and the breath sounds absent. The left lung presented normal signs. The heart was displaced to the left but there were no murmurs. Examination of the abdomen and extremities revealed nothing abnormal.

A needle was inserted into the right pleural cavity and about 50 c.c. of bloody fluid were withdrawn. Cultures of the fluid were negative, and the inoculation of this material into guinea pigs did not reveal tuberculosis. The white blood count was 28,200 per cubic millimeter with 94 per cent polymorphonuclear leucocytes. The hemoglobin was 60 per cent. The blood Wassermann reaction was negative. The sputum contained no tubercle bacilli. X-ray examination of the chest showed a homogeneous density of the lower two-thirds of the right chest. The temperature varied between 99° and 101° F. Repeated physical examinations of the chest revealed no changes. Later attempts to remove fluid from the pleural cavity were unsuccessful. The cough persisted and increased in intensity. Suddenly the patient became more dyspneic, the pulse rate rose, the blood pressure fell, and he died one hour after the onset of the change in symptoms.

Anatomical Diagnoses: Aneurysm of the lateral aspect of the ascending arch of the aorta; hemothorax; hemopericardium.

In summary, a man with pain in the chest, increasing cough and dyspnea, signs of pleural effusion on physical examination, bloody fluid obtained by thoracentesis, sudden collapse and death two months after onset of symptoms.

When the lung is invaded directly by the aneurysmal sac, there may be collapse or perforation of the lung as in Case 17. This is much more likely to occur with an aneurysm of the descending thoracic aorta where it comes in close proximity to the left lung. Another part of the lung that may be compressed is the right or left upper lobe. The signs produced by direct invasion of the lung are repeated hemoptysis or the signs of pulmonary collapse.

Pulmonary and Pleural Tuberculosis.—Tuberculosis was present in three cases. In one there was tuberculosis of the pleura due to an extension from Pott's disease. In the other two the lesions were located in the lung and were incidental findings. The tuberculosis did not occur in collapsed areas due to bronchial compression. The association of aneurysm and tuberculosis has been commented upon previously by Kortz,¹³ who collected twenty-two cases of aneurysm in combination with pulmonary tuberculosis. In the cases reported by Kortz,¹³ and also by Fraenkel⁵ and by Williams⁸ the tuberculous lesions were mostly left-sided and occurred more often when the bronchi were compressed. In four of Kortz's reported cases the tuberculosis was right-sided, and in each instance the bronchus was compressed. It is plain, however, from a study of other cases that tuberculosis of the lungs may occur in association with aneurysm without bronchial compression. Its presence, therefore, is probably a coincidental finding and has nothing to do with bronchial compression.

From the cases presented it is evident that aneurysms of the aorta frequently produce pulmonary or pleural complication through compression of the trachea, bronchi or lung, or through rupture into the lung or pleura. These features may dominate the clinical picture in such a way that the primary cause of the disturbance is overlooked.

SUMMARY

1. Twenty-two cases of aneurysm of the aorta showing conspicuous pulmonary or pleural complications are summarized.

2. Pulmonary complications, such as atelectasis, bronchopneumonia, organizing pneumonia, abscess or bronchiectasis, arise as the result of tracheal or bronchial compression or of direct invasion of the lung.

3. Pulmonary tuberculosis occasionally accompanies aneurysm of the aorta, with or without bronchial compression.

4. Pleural complications arise as a result of rupture of the aneurysm into the pleural cavity and compression of the pulmonary or azygos veins, or from extension of an infection from an underlying pulmonary lesion.

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TOTAL THYROIDECTOMY IN ANGINA PECTORIS

AN EXPERIMENTAL STUDY*

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STRIKING clinical results have been reported recently from the complete removal of the normal thyroid gland in cases of severe angina pectoris.^{1, 2} The mechanism, however, by which total thyroidectomy relieves these patients is not at all clear. The beneficial effect of thyroidectomy in the case of decompensated heart disease has been regarded as due to the resulting lowered metabolism with slowing of the circulation and consequent lessening of the burden on the heart. A close correlation has been observed in these cases between the level of the metabolism and the cardiac condition, the improvement taking place as the metabolic demands fall. This cannot be the entire explanation in angina pectoris, however, for here a beneficial effect has been observed almost immediately after operation, whereas the basal metabolic rate does not begin to fall for over a week. The following animal experiments were undertaken in the hope of assisting in the elucidation of this problem.

It has been known for some time that it is possible to produce a definite response in the unanesthetized dog by interfering mechanically with the coronary blood flow,^{3, 4, 5} and this response has been of such a nature as to convince observers that the dog experiences a sensation comparable to anginal pain in man. The experimental procedure, as described by Sutton and Lueth, consists in passing a ligature around the descending branch of the left coronary artery and bringing this out of the chest through a glass tube about which the pericardium and chest wall are closed. After the animal has recovered from anesthesia, traction on this suture compresses the vessel and the definite pain reaction is evoked.

The fact that the therapeutic effect of total thyroidectomy is observed in some cases almost immediately after operation has suggested the possibility that the procedure may in some way interfere with the sensory nerve impulses from the heart.⁶ White and his associates⁷ recently reported studies on the effect of severing various components of the sympathetic nervous system on the subsequent production of cardiac pain in dogs by the method of Sutton and Lueth. They found that the

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painful response was prevented by appropriate procedures on the sensory nervous pathways at a preliminary operation. We have similarly tested the effect of thyroidectomy upon this pain response.

METHOD

The method was essentially the same as that described by Sutton and Lueth.⁵ Under intratracheal ether anesthesia the anterior half of the fifth rib on the left was resected, the pleura was opened and a small incision made in the pericardium over the tip of the left auricle. An "E" silk suture was passed around the anterior descending branch of the left coronary vessels at this point by means of a blunt aneurysm needle and the suture brought out through a flanged glass tube. We endeavored to devise a method whereby the suture could be left in situ and the

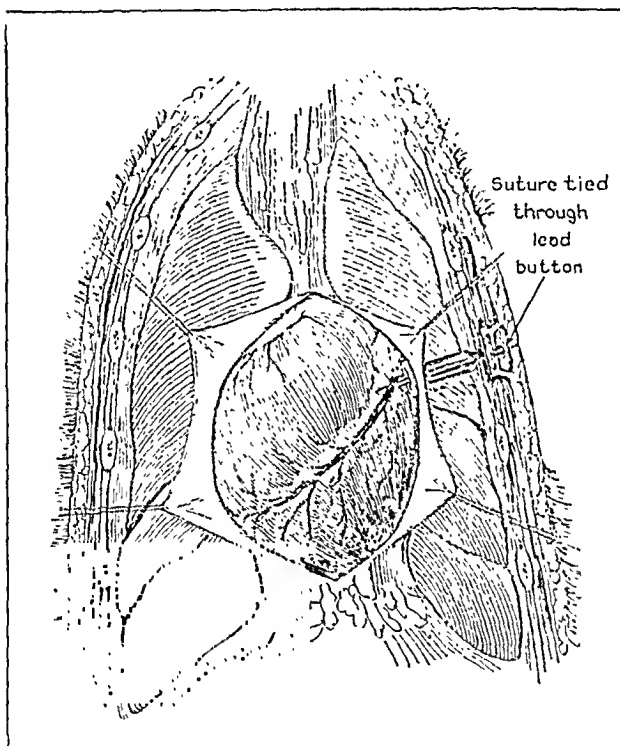


Fig. 1.—Drawing showing method for leaving coronary suture in situ, used in dog C-322.

animal retested for the pain response from time to time after thyroidectomy. This was successfully accomplished in one animal by using a short double-flanged glass tube the outer end of which was buried under the skin and subcutaneous tissues and the ends of the coronary suture anchored under the skin by a lead button (Fig. 1). At the completion of the initial operation the center of the skin wound was left open and sterile dressings were applied. Four or five hours later the dressings were removed, and the test for the pain reaction was carried out by pulling on the coronary suture with sterile instruments. The skin was now closed over the lead button and a collodion dressing applied. The test was repeated at a later date by simply making a small incision over the button under novocaine infiltration and applying traction to the coronary suture. It was found that the typical reaction could be elicited by this method quite as readily as with the proximal end of the glass tube pressed against the heart for countertraction as described by previous

experimenters. However, the procedure was found to be generally impracticable since there was invariably a low-grade fibrinous pericarditis which frequently plugged the glass tube involving the suture in organized tissue and preventing further observations. In several instances the artery became thrombosed producing an infarction of the myocardium, and in one dog the suture pulled out of the heart after occlusion and infarction had taken place. In two dogs the pleural space over the heart was obliterated by suturing the pericardium to the pleura as a preliminary operation, hoping thus to obviate the glass tube. This, however, resulted in an epicardial reaction which obliterated the landmarks, preventing an accurate placing of the coronary suture. Further efforts to leave the coronary suture in situ were abandoned, since it was felt that a preliminary control observation was not essential.*

The thyroidectomy was performed under intraperitoneal sodium pentobarbital anesthesia. Both glands were removed including the parathyroids, one or two of which were reimplanted into the sternothyroid muscle. The animals were maintained in good condition by the preoperative administration of viosterol, twenty drops daily for from ten to fourteen days,⁸ and postoperative calcium lactate 25 grams by stomach tube daily.⁹

We wish to emphasize the fact that in testing for cardiac pain the animals were not allowed to suffer needlessly. In each instance the traction on the coronary suture was released as soon as it was apparent that the typical reaction was being produced. It was found to be unnecessary to carry the stimulation beyond the point of only moderate discomfort.

OBSERVATIONS

The test for cardiac pain was made in two dogs both before and after thyroidectomy; in one this was accomplished by leaving the coronary suture in situ, and in the other by removing the suture and glass tube after the first observation and replacing them at the time of the second observation. In both dogs no demonstrable change in the response was noted after thyroidectomy.

Dog C-322. Nov. 4, 1933. Intratracheal ether anesthesia. Suture placed about coronary vessels as described above and threaded through double-flanged glass tube, the outer end of which was buried in the subcutaneous tissue. (Fig. 1.) Five hours later the animal was completely recovered from anesthesia, and traction on the suture produced definite evidence of pain on repeated observations. Wound closed; uneventful recovery.

Nov. 10, 1933. Complete thyroparathyroidectomy with reimplantation of two parathyroids into neck muscle. Moderate tetany for two days controlled with calcium.

Two weeks later. Under novocaine infiltration wound was opened over the lead button, and coronary suture readily was identified. Traction on suture again evoked the unmistakable pain response.

Six weeks after thyroidectomy. Test repeated as above, but now no response could be elicited by traction on coronary suture. Animal was sacrificed, and autopsy revealed that suture had torn out of heart and was held in fibrous pericardial

*We have found, in accord with previous observers, that the pain reaction always occurs in the normal animal provided that it is reasonably recovered from the anesthetic and that the suture includes the coronary vessels. It appears to matter little whether both the artery and vein have been included. Our suture usually compressed both vessels, but we have found that the typical reaction occurs on compression of either the artery or the vein alone.

adhesions. Surface of heart was covered with a thick, gray, jellylike exudate lying between bands of fibrous adhesions. The anterior descending coronary vessels were patent only down to the previous site of the suture and were thrombosed below this point. No gross myocardial infarction, however.

C-9. Jan. 12, 1934. Anesthesia—intratracheal ether. Suture of waxed "E" silk placed about coronary vessels as described above and threaded through a long single-flanged glass tube. Pericardial and chest wounds were tightly closed with care to remove pneumothorax. Femoral artery was cannulated for blood pressure tracings and tambour attached to chest for recording respirations. Anesthetic ceased and intratracheal tube was removed. *Thirty minutes later* dog was alert and responded in the typical manner to traction on the coronary suture. Animal was then re-etherized, intratracheal tube replaced, and glass tube with coronary suture removed. Uneventful recovery.

Jan. 23, 1934. Total thyroparathyroidectomy with reimplantation of one parathyroid into neck muscle. Dog suffered moderately severe tetany for ten days, not controlled with calcium orally and intravenously, and finally relieved by parathormone 0.5 c.c.*

Twelve days after thyroidectomy, under intratracheal ether anesthesia, chest was reopened and suture again placed about coronary vessels at the same site as before.

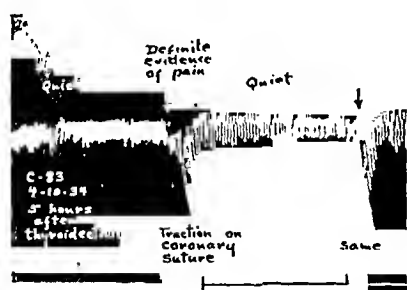


Fig. 2.

Fig. 2.—Tracing from dog C-83 showing typical response to traction on coronary suture five hours after thyroidectomy.

Fig. 3.—Tracing from dog C-12 showing typical response four weeks after thyroidectomy.

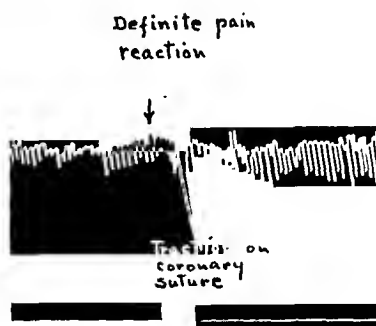


Fig. 3.

Chest was closed about glass tube. Anesthetic removed. *Thirty minutes later* the animal was alert and responded exactly as before to traction on coronary suture.

In three dogs no effort was made to test the reaction to coronary occlusion before thyroidectomy.

C-83. April 10, 1934. Morphine 0.015 grams, and intratracheal ether. Coronary suture was placed as in previous experiments and thyroparathyroidectomy performed.

Five hours later traction on the suture evoked the typical response with stiffening of the forelegs and restlessness. (Fig. 2.)

C-351. Oct. 30, 1933. Total thyroparathyroidectomy with reimplantation of four parathyroids into right neck muscle. No subsequent tetany.

Two weeks later coronary suture was placed as in previous experiments. Four hours later a definite pain reaction was produced by moderate traction on the suture.

*This was the only instance in which the viosterol and calcium regime was not effective.

C-12. Jan. 30, 1934. Total thyroparathyroidectomy with reimplantation of two parathyroids into neck muscle. Slight subsequent tetany controlled with calcium.

Four weeks later coronary suture was placed as described above. Thirty minutes after withdrawal of anesthesia traction on the coronary suture produced the typical pain response which was immediately relieved by release of the tension (Fig. 3).

It must be borne in mind, in considering these negative results on the effect of thyroidectomy, that dogs do not react to ablation of this gland in the same way as do human beings. The fall in metabolism is only temporary, the circulatory rate* is unchanged (Fig. 4), and a condition resembling clinical myxedema is very rarely observed. This is probably due to a compensatory hypertrophy of the accessory thyroid tissue which is found almost universally in the dog, scattered about the neck and upper mediastinum.¹⁰ However, the fact that the typical response to

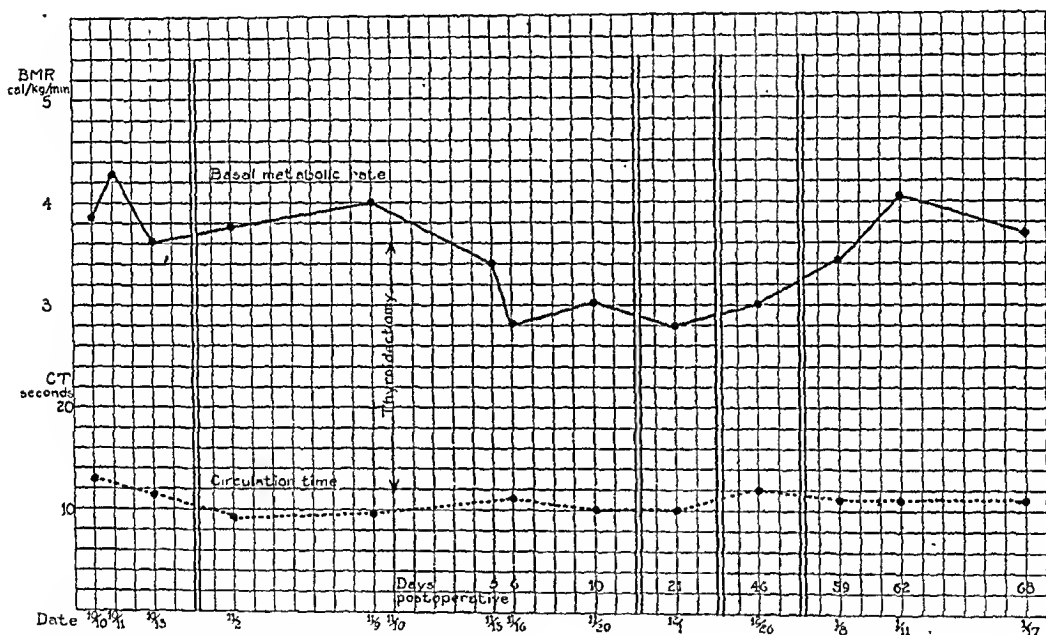


Fig. 4.—Chart on dog C-322 showing:

- (1) Spontaneous recovery from hypothyroidism due to compensatory hypertrophy of accessory thyroid tissue.
- (2) Circulation time remained unaltered in spite of a marked fall in metabolic rate.

temporary mechanical coronary occlusion can be elicited after thyroidectomy as well as before, indicates that the sensory pathways of the heart are still intact.†

COMMENT

A possible explanation of the early and dramatic change seen in angina pectoris cases after removal of the thyroid has been suggested by the

*The sodium cyanide method was used, the interval recorded between the time of injection in the femoral vein and the first deep inspiration.

†It is true that after thyroidectomy there may have been slight differences in the degree of traction required to elicit the pain response, or in the severity of the response to a given amount of traction. The limitations of the experimental procedure make it impossible to determine such minor quantitative changes. The exact experimental conditions cannot be reproduced a second time in a given animal, and the response to a certain measured amount of traction in different dogs is subject to unavoidable experimental and temperamental variations.

clinical observation of a change in reaction to adrenalin after operation. Eppinger and Levine¹¹ found that the rise in blood pressure and pulse rate induced by the intramuscular injection of 0.3 to 0.5 c.c. of 1:1,000 adrenalin was definitely diminished when the test was repeated from one to five days after total thyroidectomy; and that whereas the injection provoked an attack of angina before operation, the attack did not occur postoperatively. These authors suggested that this altered reaction to adrenalin might be responsible for the relief of anginal pain.

The interrelationship between the thyroid and the adrenals has been repeatedly demonstrated during the past twenty-five years in experimental animals. The glycosurie response to injected adrenalin has been found to be diminished after thyroidectomy.¹² Similarly the vasopressor response to adrenalin has been observed to be less after thyroidectomy¹³ and to be augmented after increasing the activity of the thyroid by electric stimulation^{14, 15} or after feeding thyroid.¹⁶ The tachycardia response to adrenalin in the isolated perfused heart has been found to be increased by thyroxin¹⁷ and decreased after previous thyroidectomy.¹⁸ This last observation has been corroborated recently by experiments on the denervated heart preparation of Cannon.¹⁹

We have studied the effect of thyroidectomy on the vasopressor action of adrenalin in dogs and found a definitely diminished response in two dogs when tested three and four weeks after thyroidectomy. However, three other dogs tested one, two, and six weeks after thyroidectomy failed to show this change. The individual variation in this regard may be due to the presence of varying amounts of accessory thyroid tissue.

The beneficial effect of removal of the thyroid gland in angina pectoris may be due, in part at least, to a diminished effectiveness of the physiological output of adrenalin. This explanation would imply that the paroxysms of anginal pain in patients with coronary artery disease may be caused by an increase from time to time in the individual's output of adrenalin. Such a concept does not seem entirely unreasonable when we reflect that the physical and emotional changes which precipitate attacks of angina are just those which have been shown experimentally to cause an outpouring of adrenalin into the blood stream.²⁰ It has been demonstrated that injected adrenalin will generally initiate an attack in patients suffering from angina pectoris;²¹ so it is quite conceivable that a sudden increase in the secretory activity of the adrenals might have a similar effect in these patients.

There are two ways in which adrenalin, either secreted or injected, might precipitate an attack of angina. First, it might cause a constriction of the coronary arteries which would directly produce the myocardial ischemia. Second, it might, by raising the blood pressure and heart rate, so increase the vascular demands of the myocardium that in

the presence of a preexisting narrowing of the coronary artery or of a rigidity preventing a compensatory dilatation, cause a relative myocardial ischemia.

Although there is some evidence that adrenalin may constrict the coronary arteries in man,²² this action has not been definitely established, and indeed it would seem a perverted mechanism which would curtail the supply of blood to the heart muscle just at that time when it is most needed. Moreover the atheromatous condition of the coronary arteries, which is frequently observed postmortem in patients suffering from angina pectoris, makes it improbable that in these patients an active vasoconstriction could have been the cause of the attacks.

On the other hand, there is considerable clinical evidence that an increase in the work of the heart may be the precipitating factor in many cases of angina. There have been reported recently several careful clinical studies^{23, 24, 25} which indicate that a rise in blood pressure and increase in heart rate are very frequently associated with the attack of angina, and some clinicians have ventured the opinion^{24, 25} that these circulatory changes do not take place as a result of the painful attack, as has been believed, but are rather the immediate cause of the attack.

The "experimental angina" produced in dogs by Sutton and Lueth's method depends upon a constriction of the coronary vessels, with the demands of the heart muscle remaining constant; however, as we have demonstrated, there are certain objections to the clinical application of this mechanism. In a previous communication²⁶ experimental observations have been presented describing a method for eliciting the same pain response in the unanesthetized dog by suddenly increasing the work of the heart in the presence of a constant slight narrowing of the coronary vessels. This was accomplished by establishing a constant subminimal pull on the coronary ligature by means of a weighted cord and then injecting a vasopressor dose of adrenalin into the femoral vein. The reaction which has been found to indicate cardiac pain in the dog was observed to occur coincidental to the rise in blood pressure. Adequate control studies showed that the subminimal traction alone or the adrenalin alone would not cause pain.

We have studied the effect of thyroidectomy upon the production of cardiac pain by the above method. Although it was possible to elicit the response in thyroidectomized animals, it soon became apparent that the experimental method did not lend itself to an accurate evaluation of this factor. One difficulty was that the vasopressor response to a given dose of adrenalin differed so widely in the various dogs tested that it would have been necessary to repeat the test for cardiac pain before and after thyroidectomy in the same animal. It was obviously impossible

to reproduce the experimental conditions a second time in the same dog with sufficient accuracy to warrant definite conclusions. Even if the suture were successfully left in situ, the local reaction in the cardiac tissue would inevitably alter the amount of tension required to produce a given amount of constriction.

SUMMARY

Thyroidectomy does not alter the pain response in dogs produced by mechanical interference with the coronary blood flow.

The possibility is discussed that the beneficial effect of total thyroidectomy in angina pectoris may be due to an interference with the thyro-adrenal mechanism.

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INTERLOBAR EFFUSIONS IN PATIENTS WITH HEART DISEASE*

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INTRODUCTION

EFFUSIONS in the interlobar spaces of the lungs are much more frequent in patients with heart disease than has been considered heretofore. The diagnosis was not made with any degree of certainty until correlated studies with x-ray and autopsy findings were made.^{1, 2} Since then several individual case reports³⁻⁸ of such effusions occurring in the course of congestive heart failure have appeared in the literature.

We have reviewed the clinical course of 18 patients with interlobar effusions who have been on the wards of Montefiore Hospital since 1930, and in this study we wish to stress the comparative frequency with which the condition is encountered and its relationship to the general problem of myocardial insufficiency.

PATHOGENESIS

On purely theoretical grounds, any inflammatory reaction which involves the lung parenchyma or the pleura may give rise to an interlobar effusion, provided the disease process is close enough to the fissure. In heart disease the effusion may arise as an exudate from a pleurisy or pericarditis in the course of active rheumatic fever; it may follow an infarction along a pleural surface, or it may occur during cardiac decompensation. The reason for the localization in the latter condition is not quite so apparent, because here it is the result of transudation from congested lungs and pulmonary stasis, a purely mechanical process.

In the pathological studies of Steele,⁵ Keiser,³ and Austrian,⁸ the outstanding finding was an adhesive pleurisy which completely obliterated the pleural sac except in the area destined to house the fluid (the interlobar region). These writers concluded that fluid entered into the interlobar space during congestive failure for one very simple reason—it had no other place to go. In most of the cases reviewed, as in ours, an antecedent history of pneumonia or pleurisy could not be elicited to explain the obliteration of the pleural sac. However,

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pleural reactions are very common in decompensated cardiacs and, as a result of repeated bouts of failure, they lead to thickenings which become appreciable radiographically in the costophrenic sinuses and interlobar fissures, and may go on to the formation of adhesive bands between the two pleural layers. It seems logical to attribute the picture to pleuritides of this nonspecific nature, upon which are often superimposed congelation and fibrin deposition from chest fluid as a result of chronic stasis.

The interlobar fissure appears to be least affected by these pleural reactions for several reasons: first, because pleurisy most commonly involves the two layers forming the free pleural cavity; second, with respiration a pleuritis spreads very easily by contiguity as a moving structure (the lung) expands and contracts against the relatively fixed costal cage. The pleura on either side of the interlobar fissure, however, tends to remain in contact. Third, drainage of fluid from the interlobar region is facilitated by the two areas of lung surface in contact with it, while drainage from the pleural cavity cannot be so efficient, as the effusion is bounded on one side by the chest wall. Fourth, the amount of fluid is generally much less than in the free pleural cavity; hence resorption is again more rapid and more complete.

While this undoubtedly explains the well-marked cases with typical textbook appearance, there exists another and more common group. Here the obliterative pleurisy is not at all prominent, and transudation of fluid takes place both into the general pleural cavity and into the interlobar pleural space. The hydrothorax rising in the chest cavity indents the pleura and lung tissue on either side of the fissure due to mechanical pressure, and additional fluid seeps into the interlobar pleural space. At times it is difficult to differentiate between these two layers of fluid. Studies of such cases have made us suspect that in many patients with cardiac decompensation, in whom hydrothorax of the general pleural cavity occurs, there is at the same time an effusion in the interlobar space.

ANATOMY AND ROENTGENOGRAPHY

A knowledge of the anatomy of the interlobar fissures is essential for a clear understanding of the physical changes that are encountered. On each side there is an oblique fissure which transects the lung almost to the hilum, and a transverse fissure which lies only on the right side, separating the upper from the middle lobe of that lung. As Brown⁹ points out: "each oblique fissure is at right angles to the lateral chest wall, while the transverse fissure is at right angles to the anterior chest wall. Hence thickening or fluid in the oblique fissures is best observed in the lateral view; whereas thickening or fluid in the horizontal fissure is most readily recognized in the anteroposterior position." (Fig. 1.)

The radiological picture depends upon the position of these pockets of fluid, whether they lie closer to the anterior, the posterior, the medial or the lateral portion of the fissure. The x-ray diagnosis has



Fig. 1.

Fig. 2.

Fig. 1.—Case 1, admission plate showing large effusion in the transverse fissure.

Fig. 2.—Case 1, after one week of diuretic therapy; only an interlobar fissure scar remains.

Fig. 3.

Fig. 4.

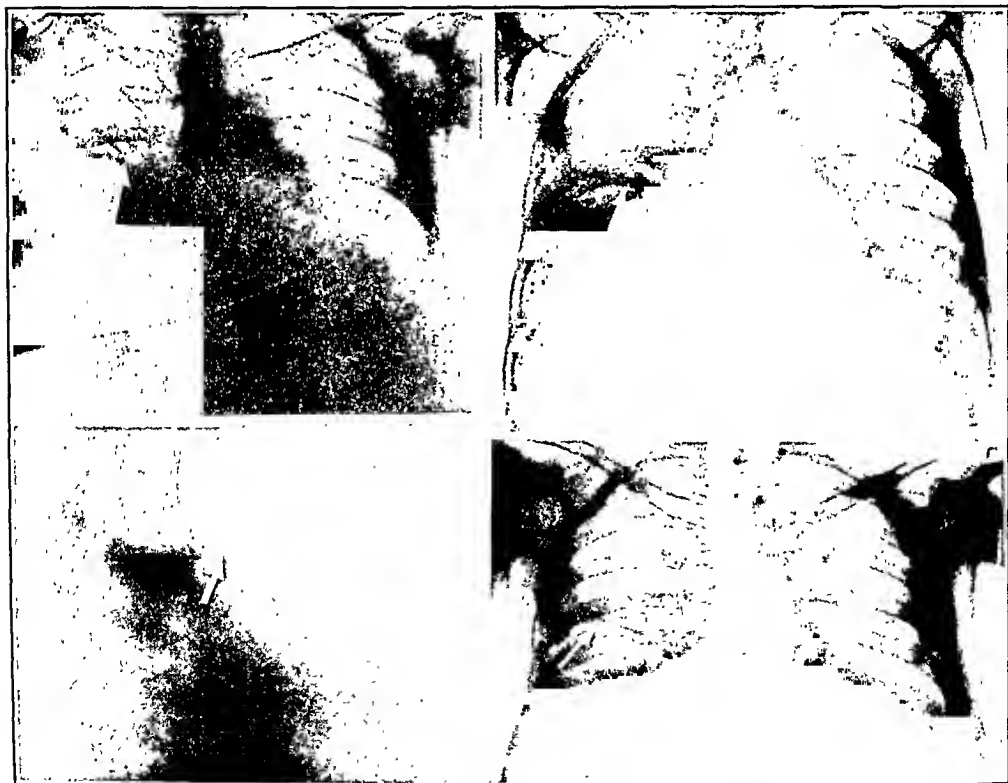


Fig. 5.

Fig. 6.

Fig. 3.—Case 2, on admission, in the x-ray film fluid in the general pleural cavity obscures the interlobar effusion which is present. Satisfactory evidence of its presence was revealed by fluoroscopy.

Fig. 4.—Case 2, after one week of diuretic therapy.

Fig. 5.—Case 2, lateral view taken at the same time as Fig. 4, to show the relation of the effusion to the interlobar fissure.

Fig. 6.—Case 2, general clearing two to three weeks after diuretic therapy. Only a thin layer of fluid remains in the interlobar fissure with much more in the free pleural space.

been too well described to warrant detailed description in this communication, suffice it to say that the shadow may be band-shaped, wedge-shaped, elliptical or round, depending upon the amount of distention and the area of pleural surface involved. Bending for-

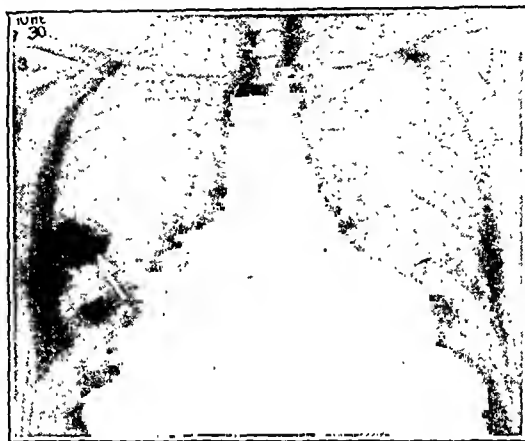


Fig. 7.—Case 6, sacculated effusion in the transverse fissure. The white arrows indicate the fractured ribs on the opposite side.



Fig. 8.—Case 14, effusion into the fissure between the azygos and upper lobes of the right lung.

ward, backward, or from side to side, frequently will accentuate the shadow of an interlobar effusion.

REPORT OF CASES

The patients were all chronic cardiac individuals. They were studied by combined fluoroscopic and roentgenographic examination,

INTERLOBAR EFFUSIONS AS A RESULT OF TRANSUDATION

CASE	DIAGNOSIS	FINDINGS	AFTER THERAPY	COMMENT
No. 1 C. B. 36, 0	CRCVD, MI, MS, AI, AS,* complete a-v dissociation, con- gestive failure.	Ovoid effusion into transverse fissure (Fig. 1). Diaphrag- matic adhesions and obliteration of costophrenic angle present—indicate the exten- sive pleural reactions which result from long-standing decompensation.	Complete disappearance of ef- fusion (Fig. 2): Note thick- ened interlobar pleura.	When taken off diuretic meas- ures, symptoms returned. Daily fluoroscopic studies showed dramatically the re- accumulation of interlobar fluid. Therapy again pro- duced resorption.
No. 2 S. H. 44, 0	CACVD,† hypertension, dia- betes mellitus, R.S.R., conges- tive failure.	Homogeneous density through- out right lower chest revealed by x-ray picture; by fluoros- copy, however, a denser layer above the free fluid in region of transverse fissure was ob- served (Figs. 3, 4, 5).	Resorption first in interlobar region and to a lesser de- gree from general pleural cavity. Marked clearing about two to three weeks after admission. (Fig. 6.)	Coexistence of effusion in dif- ferent locations is here demonstrated. Chest fluid in individuals with myocardial failure will fill all the poten- tial spaces, if present in suf- ficient quantity.
No. 3 I. L. 30, 0	Congestive heart failure, R.S.R., etiology?	Small sacculated effusion into transverse fissure.	Disappearance, leaving only faint scar.	Reappearance and resorption of interlobar fluid in subsequent breakdowns with same di- uretic measures.
No. 4 G. S. 22, 0	CRCVD, MI, MS, AI, AS, auricular fibrillation, conges- tive failure.	Free fluid in right chest ex- tending into transverse fis- sure and limited from going above this by pleura ad- herent to lateral chest wall.	Disappearance of free and in- terlobar fluid.	
No. 5 S. L. 56, 0	CACVD, hypertension, intra- ventricular conduction dis- turbance, congestive failure.	Free pleural fluid with small effusion into transverse fis- sure.	Almost complete resorption.	
No. 6 J. D. 60, 0	CACVD, hypertension, R.S.R., auricular flutter, congestive failure.	Extensive pleural thickening in lower right chest with small, rounded effusion tapering at the ends, representing an effusion into the transverse fissure. (Fig. 7.)		Three broken ribs were present on left side and these, in as- sociation with the round shadow, might have been diagnosed as pulmonary neo- plasms with metastases and pathological fracture.

*CRCVD, Chronic rheumatic cardiovascular disease; MI, mitral insufficiency; MS, mitral stenosis; AI, aortic insufficiency; AS, aortic stenosis; R.S.R., regular sinus rhythm.

†CACVD, chronic arteriosclerotic cardiovascular disease.

TABLE I—CONT'D

CASE	DIAGNOSIS	FINDINGS	AFTER THERAPY	COMMENT
No. 7 S.M. 62, 0	CACVD, congestive failure, R.S.R., pulmonary emphy- sema, chronic bronchitis.	Moderate increase in lung markings due to congestion. Small effusion, hemispherical in shape, into transverse fis- sure.		
No. 8 M.L. 63, 0	Hypertensive heart disease, R.S.R., congestive heart fail- ure.	Small amount of fluid and pleural thickening in right costophrenic angle. Saccu- lated effusion into transverse fissure.	Markedly decreased.	
No. 9 A.D. 63, 0	CACVD, multiple myocardial infarcts, R.S.R., congestive heart failure.	Free fluid in right chest dip- ping into transverse fissure. Thickening in left costo- phrenic angle.	Complete disappearance.	
No. 10 B.S. 33, 0	CROVD, MI, MS, R.S.R., con- gestive failure.	Moderate amount of fluid at right base with thin bandlike layer in transverse fissure.		Appears nicely in contrast to layer of fluid which extends over it from general pleural cavity.
No. 11 E.P. 43, 0	Acromegaly, osteitis fibrosa cystica, R.S.R., CACVD.	Thin band of effusion into transverse fissure.		No other sign of decompensa- tion present.
No. 12 E.W. 40, 0	CROVD, MI, MS, auricular fibrillation, congestive heart failure.	Small amount of fluid at right base with thin ribbon of fluid into transverse fissure.	Interlobar scar and thickening in both costophrenic angles.	
No. 13 M.deP. 14, 0:	CROVD, MS, AS, AI, R.S.R., congestive heart failure.	Marked thickening of left oblique fissure in lateral view.		Fissure involvement of left side is unusual. In this case the anteroposterior view is nega- tive.
No. 14 J.N. 49, 0	CROVD, AI, AS, MI, MS, R.S.R., cardiac decompensa- tion.	Extensive pleural effusion at right base and a thin film ex- tending along the lateral chest wall to the apex and dipping into the fissure of the azygos lobe (Fig. 8).	Resorption by tap and diuretic therapy.	This case is unique. The azygos lobe is an anatomical anomaly and its association with interlobar effusion is even more rare. ¹⁰

TABLE II
INTERLOBAR EFFUSIONS AS A RESULT OF EXUDATION*

CASE	DIAGNOSIS	FINDINGS	AFTER THERAPY	COMMENT
No. 15 B. F. 36, 0	Chronic diffuse glomerular nephritis (nephrotic stage), hypertension, enlarged heart, anasarca.	After admission, patient developed an inflammatory process in right lower chest with effusion into adjacent transverse fissure.	With recovery from acute infection and restoration of compensation, both lung fields became clear.	Interlobar fluid here appears to be due to a combination of three factors: (1) inflammatory reaction from bronchopneumonia (?), (2) mechanical transudation, and (3) capillary wall damage.
No. 16 R. E. 40, 0	Rheumatic polyarthritides, auricular fibrillation, R.S.R., erythema multiforme.	Diffuse pleuritis in lower left chest. Small oval effusion into oblique fissure. Process progressed with effusion spreading to general pleural cavity (Fig. 9).	Upon subsidence of activity, the interlobar effusion cleared up. Free fluid removed by tap.	The effusion and its unusual location are on basis of a rheumatic pleuritis.
No. 17 R. McC. 41, 0	CRCVD, MI, MS, relative tricuspid insufficiency, R.S.R. with extrasystoles, congestive failure, pulmonary infarction	Rough friction rub in anterior chest on physical examination. Extensive pleural thickening in right costophrenic angle and in interlobar fissure with small amount of fluid in latter.	Gradual improvement.	Pulmonary infarction.
No. 18 S. M. 18, 0	CRCVD, AI, AS, MS, tricuspid insufficiency, first degree heart-block, congestive heart failure, pulmonary infarction.	Area of infarction in right middle lobe with effusion into transverse fissure.	After 5 days beginning resorption; after 24 days complete resorption.	Pulmonary infarction with its presence demonstrated at autopsy.

*Since the original investigation, 8 additional cases have come to our notice. Seven of these belong to the transudative group and one (the result of infarction) falls into the exudative group.

a procedure which is superior to taking plates alone for the detection of effusions which are small or which mingle intimately with shadows produced by other structures in the chest. (The individual case reports are given in table form.) From these tables, it can be seen that interlobar effusions fall into two main groups—the transudative and the exudative types. In the first group are included the single isolated effusions (which develop in the interlobar region because of adhesions closing the general pleural space), and the interlobar effusions coexisting with free fluid in the general chest cavity and representing extensions from it. (Cases 2, 4, 5, 9, 10, 12, 14.) In the exudative type of interlobar effusion we have those resulting from specific inflammatory reactions, such as infarction, rheumatic pleuritis, etc.

These patients illustrate the frank types of interlobar hydrothorax. The most striking thing, however, was to find linear shadows or scars



Fig. 9.—Case 16, an interlobar effusion into the left oblique fissure, a very unusual location.

in the interlobar regions of more than 75 per cent of several hundred cardiac patients examined. Because of its position, thickening of the transverse fissure offers such a striking contrast to the surrounding lung as to make it easily recognized. In addition there was usually thickening of the parietal pleura, diaphragmatic adhesions, and obliteration of the costophrenic angles. These structural changes can mean only one thing in the light of a history of repeated bouts of decompensation—that fluid has collected and has been resorbed in these areas on one or more occasions, leaving its sequelae.

DISCUSSION

There are many points of interest about an interlobar effusion aside from its mere physical presence. In nearly all of the cases studied the

effusion was on the right side. This is not at all fortuitous, because it is also true of effusions into the general pleural space. Second, physical signs are comparatively few, and the condition is usually an accidental finding in the teleroentgenogram. Attempts to verify the diagnosis by puncture are extremely unsatisfactory. Their rapid disappearance with treatment is characteristic and refutes the common conception that diuretic measures are of no avail in the mobilization of chest fluid. This in general may be true of the ordinary type of hydrothorax, but it does not apply to interlobar fluid. The difference between the two probably lies in the fact that the total fluid area involved is much less, and that the two areas of lung tissue which bound the fissure form a more active resorption surface.

The relationship of auricular fibrillation and diseases of the aortic valve to this condition has been stressed by certain writers.^{6, 8} We feel that these are coincidental and are merely expressions of long-standing cardiac disease associated with decompensation.

Differentially, lung abscesses, tumor nodules or pulmonary infarcts may closely resemble interlobar effusions, and confusing shadows may be cast by the pectoralis and trapezius muscles, or by localized thickening of the pleura in the general pleural cavity. As a rule, however, a density of this sort in a decompensated individual, which seems to melt away with the return of compensation, should present no great diagnostic problem.

SUMMARY

Although interlobar fluid accumulation has a varied etiology, it is most frequently encountered in patients with heart disease. In this condition it may be the end-result of an inflammatory process or, more commonly, it may be the transudative type found in decompensated individuals.

Interlobar effusions arising by transudation differ in no way from those in the free pleural cavity except in location. Some are walled off in the interlobar region by an adhesive pleurisy of the general pleural space; others merely enter the fissure as an extension from a hydrothorax.

In the course of heart failure pleural reactions are very frequent, not only in the interlobar region but also in the free pleural space. Upon resorption, only scars or thickened pleura remain. Whenever such residua are found, it is reasonable to assume that the patient had either preexisting fluid (interlobar or otherwise) or chronic pulmonary stasis.

Interlobar effusions and their pleural thickenings are not roentgenological freaks, but constitute an integral part in the history of chronic cardiac disease.

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ADHESIVE MEDIASTINOPERICARDITIS WITH NORMAL CARDIAC ELECTRICAL AXIS ROTATION ON POSTURAL CHANGE

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EINTHOVEN¹ observed that when the body of a patient was rotated from right to left, a change in the form of his electrocardiogram took place. This change represented a shift in the electrical axis of the heart. Einthoven originally attempted to measure the action current of the beating heart as a succession of vectors. He devised the three leads graphically represented by the sides of an equilateral triangle.

The representations of the ventricular impulses of the three leads, recorded simultaneously, were assumed to record the summation of the electrical potentials of the entire mass of the ventricular muscle. The direction assumed by the vector representing this summated electrical potential was termed the electrical axis. The zero degree position of the circle, from which the axis position was measured, was arbitrarily placed pointing directly caudad. Rotation to the left was indicated as negative degrees and to the right as positive degrees, the maximum being the 180 degree point which lay directly cephalad.

In spite of the failure to record simultaneously all three leads, it has been a generally accepted procedure to estimate this electrical axis by calculation from the algebraical summation of the greatest positive and negative deflections of the QRS complexes in Leads I and III.

The change in the electrical axis with shift of position of the patient was interpreted by Einthoven as being due to a rotation of the heart in the chest about the longitudinal axis of the body. This change has been commonly regarded as being absent in patients with chronic adhesive mediastinopericarditis. By this term we mean that state in which firm, chronic inflammatory adhesions exist between the heart and the pericardium, and between the pericardium and the adjacent mediastinal structures and the chest wall. The belief that axis fixation occurs in this type of pericardial disease is based largely on the observations of Dieuaide.² This investigator reported two cases in which at post-mortem examination dense adhesions were found to exist between the heart, the pericardium and the mediastinum. These patients, during life, had

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†We are indebted to Miss Ola Nagle and Miss Jane Wasserman for technical assistance.

shown no shift of the cardiac electrical axis with rotation of the body. Dieuaide's study also included two additional patients in whom there was a very slight axis change and in whom at necropsy there was a moderate fixation of the pericardium and mediastinum. Eight other cases showed clinical signs of adhesive mediastinopericarditis, but normal axis rotation was found. None of these latter eight patients had combined mediastinopericardial adhesions at autopsy, although chronic adhesive mediastinitis or pericarditis may have existed separately. Dieuaide hoped to diagnose only instances of adhesive pericarditis in which adhesions involved both the mediastinum and the pericardial cavity.

The purpose of this report is to show the behavior of the electrical axis of the heart in extensive chronic adhesive pericarditis with medi-

TABLE I
ROTATION OF THE ELECTRICAL AXIS OF THE HEART IN NORMAL SUBJECTS

SUBJECT	SEX	AGE (YEARS)	SHIFT* (DEGREES)
1	F	50	5
2	M	32	7
3	M	25	11
4	F	28	12
5	F	35	13
6	M	65	13
7	F	26	15
8	F	56	17
9	M	8	18
10	M	65	20
11	F	24	21
12	M	15	23
13	M	20	25
14	F	22	28
15	M	27	28
16	F	15	28
17	M	21	44
18	M	27	55
19	F	11½	64

*"Shift" represents the difference in degrees of the electrical axis of the heart as measured in the right lateral and left lateral positions.

astinitis, based on a study of five cases. The diagnosis was proved by autopsy in four, and by operation in one. It was hoped that by correlating the electrocardiographic with the pathological and operative findings the relative value of the electrical axis shift in the diagnosis of adhesive disease of the pericardium and mediastinum might be ascertained.

TECHNIC

The technic employed was that of Dieuaide. It consisted of estimations of the shift of the electrical axis from electrocardiographic tracings taken with the patient (1) in the dorsal recumbent position, (2) in the right lateral recumbent position, and (3) in the left lateral recumbent position. In some of the cases records were made in this way, then repeated in both full inspiration and full expiration.

The calculation of the electrical axis was made by the use of the graphic representation of Einthoven's formula prepared by Carter, Richter and Greene.³

RESULTS ON NORMAL SUBJECTS

Dieuaide estimated a normal shift of the cardiac electrical axis by inspection of the electrocardiographic tracings. No one, to our knowledge, has assigned numerical values to these axis shifts. By the use of Dieuaide's technique, a group of normal individuals varying in age from fifteen months to sixty-five years was studied. The results are tabulated in Table I, and show a normal variation of from 5 degrees to 55 degrees shift in axis.

With this wide normal range and especially with the occasional instances of 11 degrees to 13 degrees axis shift, it is obvious that fixation of electrical axis must be within the range of 5 degrees to be of any abnormal significance, which is practically within the error of electrical axis measurement.

RESULTS ON PATIENTS WITH CHRONIC ADHESIVE MEDIASTINOPERICARDITIS

The cases studied were limited to those in which proved adhesive mediastinopericarditis was present and in which the electrical axis shift was measured. A comparison could then be made with the accepted values of normal, and with the results obtained in normal subjects by ourselves. The technique used in each case was the same.

The following brief summaries indicate the nature and extent of the pertinent anatomical findings in four patients with chronic adhesive pericarditis as revealed by operation in one case, and by autopsy in the remainder of the cases; and one case (with autopsy) of carcinomatous and inflammatory invasion of the pericardium and mediastinum.

CASE 1.—R. B., female, aged thirty-eight years. Dr. A. L. Brown removed the medial portions of the third, fourth and fifth left costal cartilages at operation. (Oct. 22, 1932), and the following findings were disclosed:

The pericardium was calcified, thickened, and adherent both to the myocardium and to the anterior chest wall. The thickened pericardium could not be separated from the underlying heart muscle. The clinical and postoperative diagnoses were: chronic adhesive mediastinopericarditis, calcified, right hydrothorax, auricular fibrillation and congestive heart failure. In this case there had been an axis shift of 20 degrees on May 4, 1931, but only 9 degrees on February 15, 1934, about sixteen months after operation. (Fig. 1.)

CASE 2.—E. S., male, aged forty years. (Autopsy Nov. 27, 1932, by Dr. A. Nemir.) There were adhesions present between the right border of the pericardium and the mesial borders of the lower and middle lobes of the right lung. Adhesions were also present between the pericardium and the thoracic cage to the right and left of the sternum as well as the contiguous pleura of the left lower lobe. The pericardial cavity was obliterated by dense adhesions. The anatomical diagnoses were: chronic adhesive mediastinopericarditis; rheumatic heart disease with aortic

insufficiency, mitral insufficiency and stenosis; right bundle-branch block; pulmonary infarction and bronchopneumonia. The electrical axis shift in this case on Nov. 6, 1931, was 35 degrees.

CASE 3.—E. S., female, aged fifty-four years. (Autopsy Sept. 20, 1932, by Dr. G. Y. Rusk.) The pericardial cavity was completely obliterated by dense fibrous chronic adhesions. There were dense adhesions between the right border of the

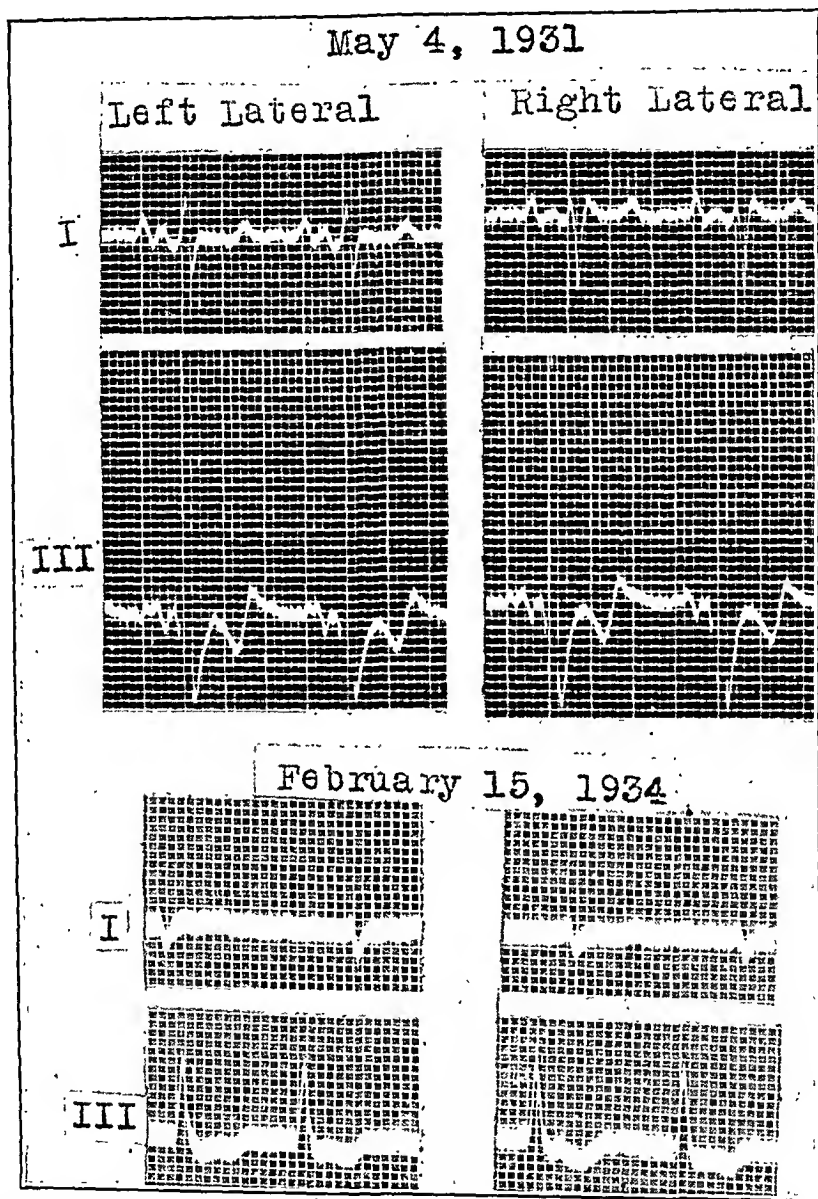


Fig. 1.—Shift in electrical axis as demonstrated by Leads I and III in the right and left lateral positions in Case 1 prior to operation and sixteen months after operation.

pericardium and the mesial borders of the middle and lower lobes of the right lung. There were also some filamentous adhesions between the pericardium and the under-surface of the rib cage. The anatomical diagnoses were: chronic adhesive oblitative mediastinopericarditis; coronary arteriosclerosis, aneurysmal dilatation of the left ventricle, cardiac hypertrophy and dilatation, atherosclerosis, bronchopneumonia and tuberculous infection of the tracheobronchial lymph nodes.

The electrical axis of this heart on April 11, 1932, shifted 42 degrees with a change in the position of the patient. (Fig. 2.)

CASE 4.—E. B., male, thirty-three years old. (Autopsy Jan. 16, 1929, by Dr. J. F. Rhinehart.) A clinical diagnosis was made of rheumatic heart disease with adhesive mediastinopericarditis. At autopsy there was found a generalized old fibrous pericarditis partially obliterating the pericardial sac with a more recent organizing fibrinous pericarditis in the free spaces with pleuropericarditis, bilateral, and adhesions from the apex of the pericardial sac to the left anterior chest wall. There was present acute and chronic rheumatic endocarditis of the mitral and aortic valves, diffuse myocardial fibroses, multiple thrombi in the left auricular appendage and infarcts of the brain, kidney and spleen. Other incidental findings were chronic passive congestion of the abdominal viscera, bronchopneumonia, and old calcified tuberculosis of the mediastinal lymph nodes.

The electrical shift in this case on June 21, 1928, was 21 degrees.

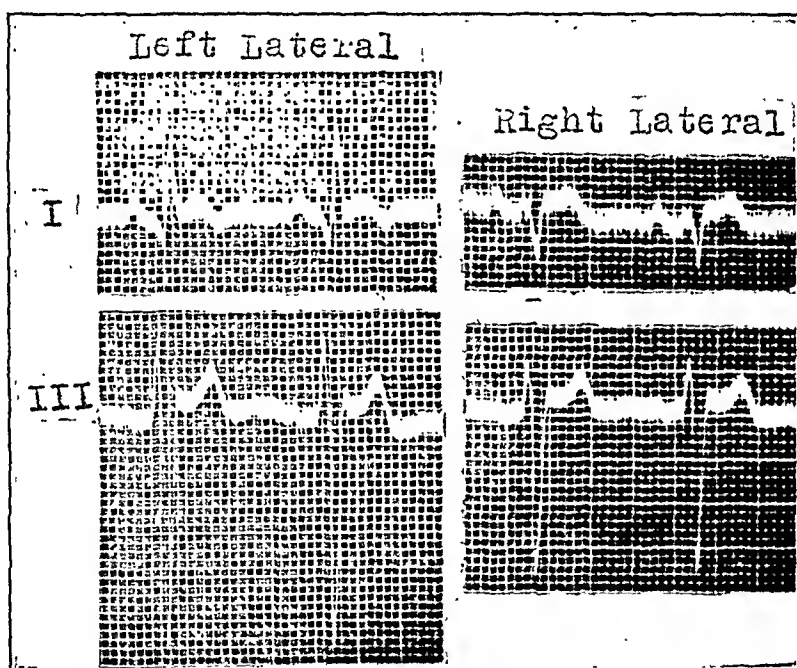


Fig. 2.—Electrocardiograms, Leads I and III demonstrating 42° electrical axis shift on postural changes (Case 3).

CASE 5.—I. B., female, aged forty-one years. (Operation by Dr. H. Brunn Sept. 7, 1927, and autopsy by Dr. G. Y. Rusk June 6, 1928.)

The history of respiratory symptoms on this patient dated from January, 1927, and the first x-ray and clinical diagnosis of carcinoma of the lung was made on July 29, 1927; and on Sept. 7, 1927, the right upper and middle lung lobes were removed. Drainage of the right pleural cavity for empyema followed, and after repeated convulsions the patient died on June 6, 1928.

The autopsy diagnosis was primary papillary adenocarcinoma of the right lung with extension into the right pleural space, the mediastinum, a portion of the right side of the diaphragm, the left lung, and the pericardium with partial obliteration of the pericardial space. There was dilatation and hypertrophy of the right auricle and right ventricle with chronic passive congestion of the abdomen, viscera and ascites and left hydrothorax. Moderate atheroma of the aortic valves, the aorta and coronary arteries and many metastases were present throughout the body. A sinus

extended through the wall of the chest into the infected pleural cavity, thence to an abscess within the mass of the tumor in the right lung.

On April 16, 1928, the electrical axis rotation on postural shift was only three degrees, well within the possible error of measurement.

DISCUSSION

An analysis of Table II shows that a normal axis rotation occurred in four of the five patients. In the one remaining case slight rotation of the axis occurred. The axis rotation in this latter case was limited to three degrees.

TABLE II

ROTATION OF THE ELECTRICAL AXIS OF THE HEART IN PATIENTS
WITH FIXATION OF THE PERICARDIUM

PATIENT	SEX	AGE (YEARS)	SHIFT (DEGREES)
1. (R.B.)	F.	38	20
2. (E.B.)	M.	33	21
3. (E.Sa.)	M.	40	35
4. (E.Sc.)	F.	54	42
5. (I.B.)	F.	44	3

Each of these five patients had extreme anatomical fixation of the heart to the pericardium and of the pericardium to the anterior and central mediastinum, pleura and the chest wall. In Case 5 there was at autopsy an almost solid block of immobile carcinomatous and inflammatory tissue binding together the heart, pericardium, pleurae, right lung, and rib cage. This was the only example of genuine electrocardiographic electrical axis fixation.

The observation made by Fenichel⁴ and others that the electrical axis shifted toward the right on turning the patient into the left lateral recumbent position was herein uniformly observed. This agrees with the conception that shifts of the heart in a frontal plane are more responsible for electrical axis shift than the rotation about the longitudinal axis. The heart assumes a slightly more prolonged form in the left lateral position than in the dorsal recumbent or erect position and a broader form in the right lateral position. This change in form coincides with the common occurrence of right electrical axis deviation in narrow-chested individuals and the reverse in broad-chested people, and possibly explains the nature of axis deviation in hypertrophy and dilatation of either ventricle rather than the theory of predominance of electrical potential developed by the greater muscle mass of the particular ventricle.

One may offer the hypothesis that the movement of the heart along a longitudinal axis is impeded but slightly by such adhesions as occurred in the first four cases reported. (Such motion was observed to give appreciable electrical axis shift.) The extensive involvement of the diaphragm in Case 5 may be the clue to the electrical axis fixation in that instance.

In certain other patients, clinically suspected of having adhesive mediastinopericarditis and not reported in this series because of lack of either surgical or autopsy confirmation of the lesion, electrical axis fixation on lateral rotation was observed, but there was a decided shift during respiration from the extreme positions of the diaphragm in inspiration and expiration. (Fig. 3.)

In these patients as well as in the five discussed in this report there was apparent anatomical longitudinal fixation of the heart as estimated

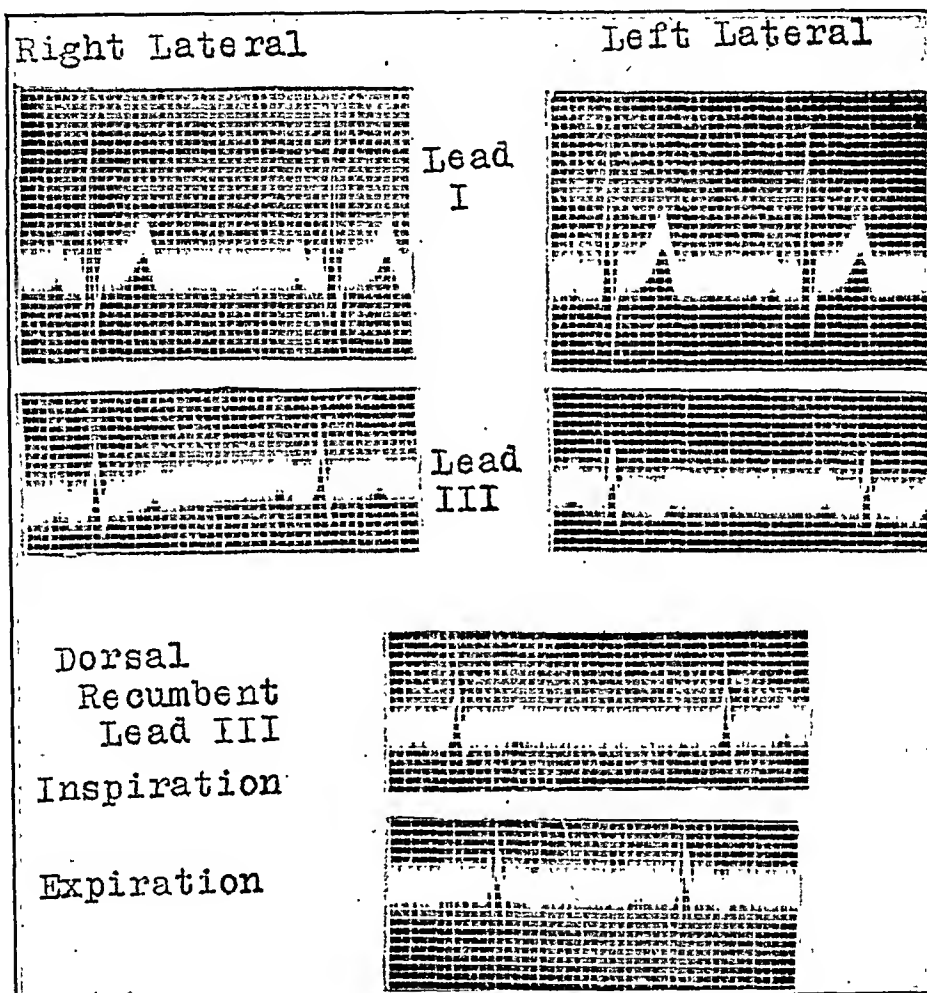


Fig. 3.—Electrocardiograms in a case of suspected adhesive mediastinopericarditis, illustrating fixation of form and electrical axis in Leads I and III on lateral posture shift, but definite difference in form of Lead III when taken in inspiration and expiration.

by constancy of position of the apex impulse, the heart border by percussion and by roentgenograms of the chest. Minor changes of the heart's position, however, are extremely difficult to estimate from roentgen ray observations. In each of the cases reported here, the position of the apex impulse of the heart as determined by palpation and percussion did not move with changes in the patient's position. This relative immobil-

ity of the cardiac apex impulse, deduced from physical examination, has served us as a far more reliable index of longitudinal axis fixation than any other means of estimate.

One may conclude from the above data that mobility of the electrical axis will not exclude extensive mediastinopericarditis but that fixation is worthy evidence of its existence probably with diaphragmatic involvement. Even this premise is not justified as a generalization, as is illustrated by the following case: a woman, aged forty-three years, (A. H.) with arteriosclerotic heart disease and hyperthyroidism with congestive failure and a large pericardial effusion showed a moderate fixation of the electrical axis (7 degrees) during acute congestive failure. Normal rotation (25 degrees) of the electrical axis of the heart was found to exist, however, following the removal of 600 c.c. of fluid from the pericardial cavity and improvement of her congestive failure.

The transient fixation in this case may have been due to the encroachment of the heart and pericardium on the other mediastinal contents and the simultaneous limitation of motion of the diaphragm by ascites and hepatomegaly.*

CONCLUSIONS

1. Normal rotation of the electrical axis of the heart may occur in patients with extensive chronic adhesive mediastinopericarditis and does not exclude the presence of this condition.
2. Fixation of the electrical axis is not pathognomonic of anatomical fixation of the heart by chronic adhesions.
3. It is suggested that when fixation does occur, the mobility of the heart has been limited in both median longitudinal and horizontal planes.

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*The influence of positions other than the right and left lateral recumbent was studied in the patient Mrs. R. B. (Case 1), and on a normal subject. The antero-posterior Lead IV of Wolferth and Wood⁵ was used as well as the standard Leads I and III.

In Mrs. R. B. the degree of change in form of the electrocardiogram caused by change in the position of the body from the right to the left lateral, was less than that caused either by the change from the supine to the prone position or by the shift of the heart incident upon full inspiration and expiration without movement of the body's position. In both this patient and the normal subject the dorsal position and the right lateral and likewise the ventral and erect positions resembled one another reasonably closely in the records of Lead IV.

TRANSIENT, RECURRENT, COMPLETE BUNDLE-BRANCH BLOCK

REPORT OF A CASE*

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THE occurrence of electrocardiograms displaying complete bundle-branch block is confirmatory evidence of well-marked heart disease. There are, however, occasional exceptions to this rule. Furthermore, the electrocardiograms of complete bundle-branch block are likely to remain remarkably unaltered during the rest of the patient's existence. Exceptions to this likewise occur. Our report deals with such departures from the rule.

Few reports regarding temporary bundle-branch block are available in the literature. In 1927 Willius and Keith reported three cases of transient, incomplete bundle-branch block occurring with heart failure and disappearing with the restitution of cardiac function. Pulmonary edema coincided with the appearance of the abnormal electrocardiographic records in two cases. Baker, in 1930, reported a case of complete bundle-branch block, occurring temporarily in an elderly man, the presence of which seemed to be related to the occurrence of auricular fibrillation and to periods of tachycardia that disappeared when the heart became slowed and also during the inhalation of oxygen. More recently Morris and McGuire reported two cases of transient, complete bundle-branch block. The first occurred in a woman aged forty-six years in an attack of pulmonary edema; the second, in a woman fifty-one years of age during acute heart failure following abdominal exploration and cholecystectomy.

The mechanism evidently responsible for the development of bundle-branch block in the six previously reported cases was that involved in myocardial changes consequent to heart failure. Wolff, Parkinson, and White have observed transient bundle-branch block in apparently healthy children and in young adults who were prone to paroxysmal tachycardia. We have from time to time observed bundle-branch block as a temporary phenomenon in the course of cardiac infarction and occasionally during the combined administration of digitalis and quinidine sulphate.

In the case forming the basis of this report none of the foregoing factors was present, which adds to the interest of the phenomenon.

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REPORT OF CASE

CASE 1.—A man, aged sixty-three years, came to the Mayo Clinic because of progressive dysuria. He had been very active and energetic, he was accustomed to assuming serious responsibilities, and he was in great demand as a public speaker. He had continued to carry these burdens and considered himself still fit to resume his strenuous and varied activities. He had been unusually well throughout his lifetime, with the exception that he had had scarlet fever in childhood and influenza in the pandemic of 1918. He complained of frequency of urination, particularly at night, and thought that he was not emptying his bladder completely. In the preceding two or three years he had been slightly short of breath on undue effort; although a year prior to his admission he had ascended a high mountain and had experienced little difficulty. There had been no anginal seizures, and no evidences of congestive heart failure had been present at any time.

Examination revealed the patient to be of average stature. The peripheral arteries were moderately thickened. The heart did not appear to be enlarged, the

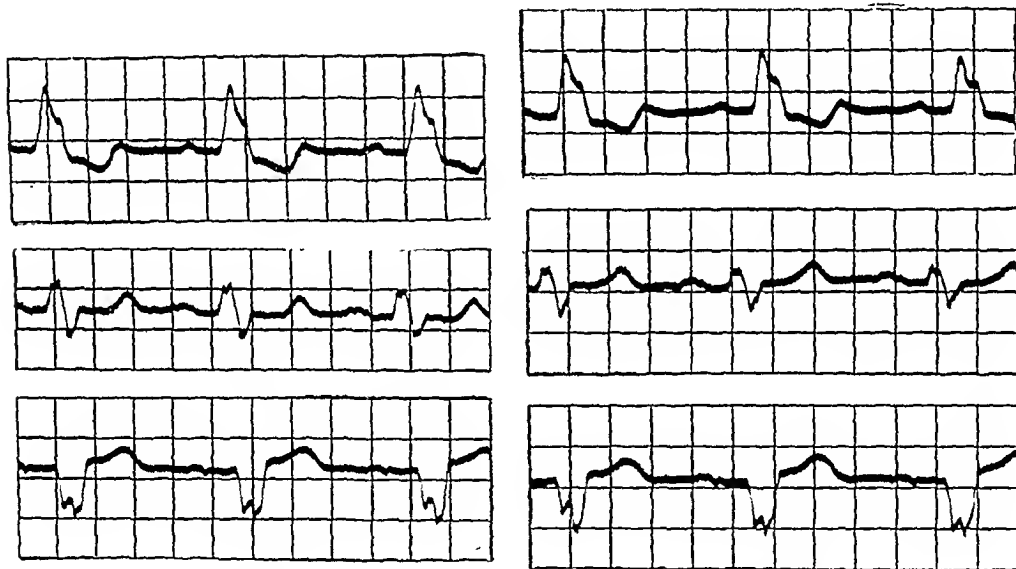


Fig. 1.

Fig. 2.

Fig. 1.—September 21. Complete left bundle-branch block; QRS intervals 0.17, 0.17, and 0.16 second. P-R interval 0.24 second.

Fig. 2.—November 13. Complete left bundle-branch block; QRS intervals 0.17, 0.17, and 0.16 second. P-R interval 0.24 second.

rhythm was regular, the tones were of good quality, no murmurs were audible, and the aortic second tone was accentuated. The prostate gland on palpation was found to be moderately, although diffusely, enlarged, and it was firm. The systolic blood pressure in millimeters of mercury ranged from 163 to 186 and the diastolic from 90 to 100. The examination otherwise revealed no important findings. Urinalysis disclosed the specific gravity to be 1.026; the urine was acid in reaction, there was no albumin or sugar present, and only a few leucocytes were found. There were 30 c.c. of residual urine. The value for hemoglobin was 14.7 mg. per 100 c.c. of blood (88 per cent Dare), erythrocytes numbered 4,500,000 and leucocytes 6,000 per cubic millimeter of blood, and the concentration of urea nitrogen fluctuated from 22 to 28 mg. per 100 c.c. of blood. Ophthalmoscopy revealed a slight degree of sclerosis of the retinal arteries of hypertensive type. A teleroentgenogram of the heart revealed no appreciable enlargement; and the electrocardiograms showed the presence of complete left bundle-branch block (new terminology). A diagnosis was

made of benign, prostatic hypertrophy, essential hypertension, and arteriosclerotic cardiac disease with complete left bundle-branch block.

Transurethral prostatic resection was performed December 19, 1933, with the patient under spinal anesthesia. There was no appreciable reaction. The patient made an uneventful recovery and was dismissed January 8, 1934.

DESCRIPTION OF ELECTROCARDIOGRAMS

The first record, obtained September 21, 1933, revealed typical, complete left bundle-branch block. The QRS intervals were 0.17, 0.17 and 0.16 second in the three

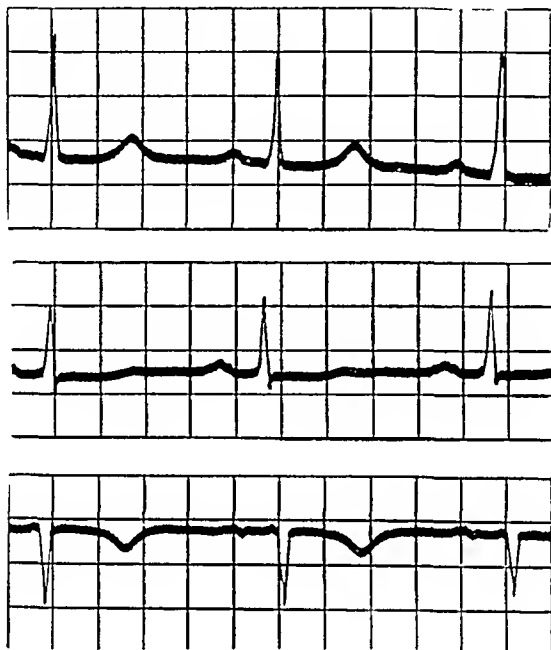


Fig. 3.—December 15. Sinus bradycardia; inverted T-wave, Lead III, prolonged S-T interval 0.38 second.

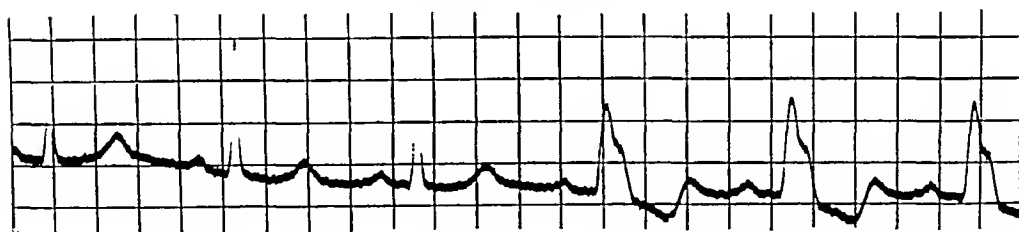


Fig. 4.—December 21. Lead I. Transition between normal rhythm and complete left bundle-branch block.

leads respectively. The ventricular components in Lead I were the mirror image of those in Lead III, and marked distortion in the contour of the QRS complexes occurred in all leads. Delayed A-V conduction also was present. The P-R interval measured 0.24 second (Fig. 1). Another electrocardiogram was taken two days later, and was identical in all respects to the one described.

It was difficult for the patient to accept the diagnosis of heart disease owing to the paucity of symptoms, and, on his return home, two electrocardiograms were taken, both of which showed the absence of bundle-branch block. This immediately raised the question of the existence of a transient abnormality, and we requested the patient to return for further observation.

He returned November 13, 1933, and the record obtained was identical with those under previous dates (Fig. 2). It then was necessary for the patient to return home, and he decided to return in a few weeks for the operative relief of the dysuria. Owing to the continued discrepancy in the electrocardiograms, he consulted still another physician at his home who made two electrocardiographic examinations; the bundle-branch block was absent on both occasions.

The patient returned to the clinic December 15, and the first tracing obtained showed the absence of bundle-branch block and delayed A-V conduction (Fig. 3). The QRS complexes were all normal in contour and time; the T-waves were inverted in Lead III and were identical mirror images of the now upright T-waves in Lead I. A prolongation of the S-T interval occurred (0.38 seconds). On the following day the bundle-branch block had reappeared. December 19 the block was absent but reappeared on the next day. December 21 we obtained an electrocardiogram showing the transition between normal conduction and complete left bundle-branch block (Fig. 4). It is interesting to observe the abruptness of these changes, occurring without intermediate configuration of the complexes. December 22 both

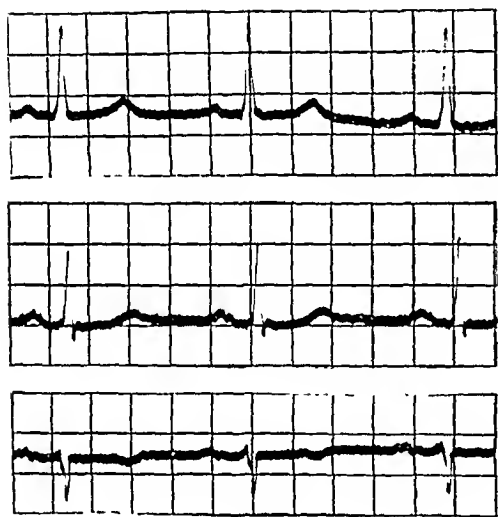


Fig. 5.

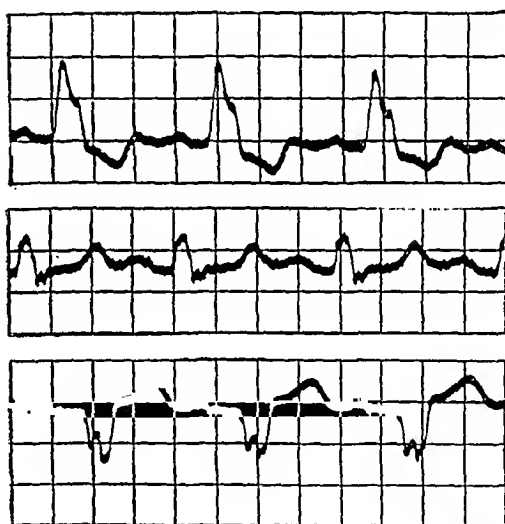


Fig. 6.

Fig. 5.—January 2, 1934. Sinus bradycardia; inverted T-wave, Lead III.

Fig. 6.—January 5. Complete left bundle-branch block; prolonged P-R interval 0.24 second.

normal and abnormal conduction occurred on two different occasions. Two records obtained December 23 revealed normal conduction. The record, January 1, 1934, showed normal conduction (Fig. 5); and the last tracing, January 5, again showed complete, left bundle-branch block and delayed A-V conduction (Fig. 6).

COMMENT

Bundle-branch block occurs most frequently, but not exclusively, with coronary disease, and the nutritional impairment thus imposed on the heart may find expression in faulty conduction. This is the presumptive explanation in this case owing to the fact that the patient's age coincides with that period of life in which coronary disease is most prevalent and to the absence of other demonstrable diseases which might have had some etiological significance.

The presence of delayed A-V conduction during the periods of bundle-branch block is interesting and indicates a rather profound and ascending interference in impulse conductivity. The fact that both bundle-branch block and delayed A-V conduction occur transiently denotes that the heart still has the ability, probably through spontaneous augmentation of its own circulation, to recover sufficiently to permit relatively normal conduction. Even though observations such as these have been made infrequently, it seems probable that transient, complete bundle-branch block is not a rare condition. It is not improbable that during the development of this abnormality periods of normal conduction may occur, and the establishment of bundle-branch block may be not abrupt but gradual; the failure in recognizing this condition as transient, complete bundle-branch block may lie in the absence of opportune electrocardiograms. This explanation also is true when applied to complete heart-block, which frequently is a transient disorder at the time of its inception.

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Department of Clinical Reports

PERICARDIAL EFFUSION FOLLOWING ACUTE CORONARY VESSEL CLOSURE*

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THE following case is of unusual interest because from a study of the literature I believe it to be the first recorded instance of pericardial effusion following an acute coronary vessel closure.

REPORT OF CASE

D. M., a Jewish male, aged fifty years, was admitted to the Montefiore Hospital on November 9, 1933. He had been perfectly well until June 10, 1933, when after a hard day's work he experienced a sharp substernal pain with radiation to the left shoulder and down to the inner side of the left arm. He took some sedative for the relief of the pain but vomited. He returned home that evening, and after two days his pain subsided somewhat, but he felt weak, perspired very freely, and suffered from marked dyspnea and gaseous eructations.

His dyspnea increased very markedly so that the only way he could obtain comfort while in bed was by sitting up with his head resting far forward on his folded arms. The patient was seen on July 7, 1933, by Ernst P. Boas, who at that time found the patient extremely dyspneic. There was dullness and marked bronchial breathing at the left base posteriorly below the angle of the scapula. The heart sounds were barely audible, and there was a to-and-fro friction rub heard best at the fourth intercostal space to the left of the sternum. In that region the heart borders percussed as far out as both anterior axillary lines. The heart rate was normal. The blood pressure was 90 systolic and 60 diastolic. A bedside roentgenogram obtained at this time (Fig. 1) revealed an unusual dilatation of the heart shadow which, in the presence of a pericardial friction rub, suggested effusion in the pericardium.

Three hundred and fifty c.c. of clear, straw-colored fluid were withdrawn from the pericardial sac with a needle inserted in the seventh intercostal space below the left shoulder blade. There was immediately very marked relief, and the patient's dyspnea disappeared gradually.

On July 26, 1933, he was admitted to Presbyterian Hospital, where a diagnosis of myocardial infarction was made. At that institution notice was taken of a bulge in the left ventricular region which was diagnosed as an intrapericardial aneurysm of the left ventricle. The character of the cardiac contour was consistent with the reaccumulation of pericardial fluid. The patient's course was prolonged by recurrences of his cardiac pain. There were several episodes suggesting fresh occlusions.

On August 21, 1933, a thoracentesis was performed with withdrawal of 350 c.c. of straw-colored fluid from the left chest. During his stay at Presbyterian Hospital

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the signs of pericardial effusion finally disappeared and the electrocardiogram showed intraventricular conduction disturbance of the bundle-branch type.

On admission to the Montefiore Hospital the patient was quite comfortable. There was no dyspnea or cyanosis of the lips. The apical impulse of the heart was in the sixth intercostal space in the anterior axillary line. There was a marked disproportion between the thrusts of the heart, which were visible, and the sounds over the same region of the apex, which were very weak. Fluoroscopic and radiographic examination of the chest showed a slight increase in the central pulmonic areas. The heart shadow showed a definite bulging in the upper part of the left ventricle, the pulsations of which were slight, wavelike, and opposite in direction to those of the pulmonic conus lying just above (Fig. 2). The left ventricle showed considerable enlargement also in the oblique view, and the bulging in its upper portion was seen to be increased and gradually disappearing when the patient was rotated in the left lateral position. The pulmonary conus itself showed only slight enlargement, while the inflow tract of the right ventricle was also enlarged. The left auricle occupied a high position on the right side forming a part of the right border in the antero-posterior view. It was not enlarged.



Fig. 1.

Fig. 2.

Fig. 1.—Bedside plate obtained on July 7, 1933, showing effusion in the pericardium.

Fig. 2.—A comparison plate obtained on November 24, 1933, when the patient was ambulatory, showing the concentric hypertrophy of the left ventricle with a bulging aneurysm in its upper border, the result of a coronary occlusion of probably the descending branch of the left. Note the absence of pericardial effusion.

After a short period of convalescence in bed the patient was encouraged to do graduated exercises so that at the present time he is ambulatory and back at work as a photographer.

SUMMARY

A case is reported of a man, aged fifty years, who developed pericardial effusion following an acute coronary vessel closure. This diagnosis was established from both clinical and roentgenographic signs. Following paracentesis of the pericardium there was great relief in symptoms, although the fluid reaccumulated subsequently. With further rest in bed and a thoracentesis the patient became well and is at present ambulatory.

PORTAL OBSTRUCTION IN RHEUMATIC HEART DISEASE WITH ADHERENT PERICARDIUM: RUPTURE OF RETROPERITONEAL VARIX WITH FATAL HEMOPERITONEUM*

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WE ARE reporting an unusual case of rheumatic heart disease with adherent pericardium and a clinical picture of portal cirrhosis in which death occurred from rupture of a retroperitoneal varix with intraperitoneal hemorrhage. Such a complication is extremely rare even in cases of true portal cirrhosis. Bezza¹ has reported hemorrhagic pseudocyst formation of the mesentery with fatal hemoperitoneum in an individual with portal cirrhosis. Déchaume² described a case with fatal intraperitoneal hemorrhage as a complication of syphilitic cirrhosis of the liver.

REPORT OF CASE

F. T., a female, aged eighteen years, was admitted to the Montefiore Hospital on January 26, 1933, with dyspnea and swelling of the abdomen as her chief complaints. At the age of seven years she had had chorea. One year later, following a sore throat and tonsillitis, she had migratory joint pains. Numerous sore throats subsequently recurred, at least once a month. A heart lesion was diagnosed at the age of eleven years when weakness and pallor were observed. In September, 1929, at the age of fourteen years, dyspnea on slight exertion was experienced, and one year later signs of congestive heart failure with slight edema of the ankles appeared. She entered a hospital where the congestive failure subsided. However, recurrent bouts of congestive heart failure necessitated numerous admissions to various hospitals for the restoration of compensation. In June, 1932, swelling of the abdomen was observed for the first time with very slight edema of the ankles. The patient was admitted at that time to another institution where six paracenteses of the abdomen were performed for recurrent ascites. Her condition gradually became worse, and she was transferred to the Montefiore Hospital as a case of chronic congestive heart failure.

Examination on admission to the Montefiore Hospital revealed an extremely ill-looking young woman, orthopneic, markedly dyspneic, with cyanosis of the lips, ears, and tip of the nose. The skin and sclerae had an icteric hue. The nasal septum revealed a large perforation anteriorly. The superficial neck veins were markedly distended and showed a totally irregular ventricular type of venous pulse. The trachea was in the midline. Over the anterior chest wall and the abdomen the superficial veins were markedly dilated, prominent, and tortuous.

The apical impulse of the heart was in the left anterior axillary line at the level of the sixth intercostal space. There was marked systolic retraction in the apical

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region; change of position did not affect the location of the apex. A diastolic thrill was felt at the apex where there was heard a rumbling diastolic murmur preceded by a rough systolic murmur. In the aortic region there were blowing murmurs throughout systole and diastole. The second heart sound in the pulmonic region was markedly accentuated and reduplicated. Auricular fibrillation with a rapid ventricular rate of 120 beats per minute was present. The blood pressure was 120 systolic and 40 diastolic. The peripheral vessels revealed a Corrigan pulse and pistol-shot sounds over the femoral arteries, but no capillary pulsations were noted. A few râles were heard at the base of the left lung. There was no evidence of hydrothorax.

The abdomen was markedly distended, with bulging of the flanks and protrusion of the umbilicus. White striae were prominent over the lower part of the abdomen. A definite fluid wave was present. The liver was very large, pulsatile, and extended down to the pelvic brim, 12 cm. below the right costal margin in the midclavicular line. The spleen was also markedly enlarged, its edge extending 4 cm. below the left costal margin.

In striking contrast to the marked ascites, the lower extremities revealed only slight pitting edema. The venous pressure was markedly elevated, 25 cm. of blood. The circulation time by the decholin method (ante-cubital vein to tongue) was markedly prolonged, 32 seconds.

There was a moderate secondary anemia with a hemoglobin count of 60 per cent (Sahli). The erythrocytes numbered 3,500,000 per cubic millimeter. The leucocyte count and differential smear were normal. The blood Wassermann reaction and the Kahn precipitin test were negative. The blood serum albumin was 3.50 and the serum globulin 1.72 grams per 100 cubic centimeters of blood.

X-ray and fluoroscopic examinations of the chest revealed marked enlargement of the left ventricle and of the left auricle, part of the left auricle appearing on the right border of the heart when viewed in the anteroposterior position. There was moderate enlargement of both the inflow and the outflow tracts of the right ventricle. No definite enlargement of the right auricle could be demonstrated. Several areas of infiltration in the right infraclavicular region and one in the right mid-zone region were interpreted as indicative of pulmonary infarctions. The central pulmonic vessels were very prominent.

The electrocardiogram showed auricular fibrillation with right axis deviation.

Course in the hospital: During her stay in the hospital the patient became progressively worse. She required paracenteses of the abdomen from one to three weeks apart, each one yielding 5 to 12.5 liters of fluid. Cultures of the abdominal fluid were repeatedly sterile. Despite the massive ascites, edema of the legs was always minimal. During the first two months in the hospital her temperature was normal, aside from an occasional transitory rise to 101° F. Thereafter, however, a low grade fever persisted with rises up to 101° F., for which no adequate explanation could be found aside from the assumption that rheumatic activity was present. Occasionally a hacking cough was noted, but no expectoration was produced. Four months after admission the temperature gradually rose to 103° F., and thereafter varied from 99° to 103.2° F. A blood culture obtained during this period was negative.

In the middle of May, 1933, she developed mild diffuse abdominal pains following the removal of nearly 11 liters of ascitic fluid at one time. Marked diffuse abdominal tenderness was elicited, but there was no rigidity. The pains persisted, the umbilicus became red, and an exploratory puncture of the abdomen yielded a homogeneously bloody fluid, culture of which was sterile. Because of the numerous varices in the abdominal wall, it was suspected that one of these veins had accidentally been

punctured during the last paracentesis. Her abdominal symptoms gradually disappeared. Two weeks later, on June 2, 1933, the patient suddenly died while asleep.

Necropsy.—(Only the important findings will be detailed.) The peritoneal cavity contained 2 liters of homogeneously bloody fluid. A large hematoma, 7 to 8 cm. in diameter, was found in the lateral wall of the right side of the abdomen just beneath the parietal peritoneum. It overlay a very markedly distended and partially thrombosed vein which had ruptured. The hematoma had ruptured into the peritoneal cavity at one point. The veins on the inner surface of the abdominal wall and those in the retroperitoneal region were distended and tortuous.

The heart was very large, weighing 1,100 gm. The pericardial sac was completely obliterated, and the inferior vena cava was partially constricted and embarrassed by adhesions as it entered the pericardial sac. Dense adhesions to the diaphragm were present. Microscopic examination revealed marked thickening with vascular fibrous tissue. The left ventricular wall measured 19 mm. and the right ventricular wall 6 mm. The myocardium revealed marked hypertrophy of the muscle fibers with numerous scars throughout, some deeply hyalinized. All the chambers of the heart were markedly distended. The aortic valve showed rolling and shortening of the anterior and mesial leaflets with slight fusion of their commissures. The mitral valve was only slightly thickened along the line of closure in the lateral leaflet. The chordae tendineae were somewhat shortened and the papillary muscles considerably hypertrophied. Although the left auricle and pulmonary veins were enormously distended, the pulmonic conus was about normal in size. The tricuspid valve was slightly thickened and the lateral leaflet somewhat rolled. The papillary muscles were hypertrophied. The valvular measurements were: aortic ring 7.5, mitral ring 15.5, pulmonic ring 7, and tricuspid ring 16 cm.

The right lung presented a few adhesions over the lateral portion of the upper lobe. A deep irregular scar in the lower portion of this lobe was apparently the residuum of an old infarct. A triangular wedge-shaped area of consolidation extended from the hilum to the periphery of the upper lobe. Throughout this area numerous small tubercles and several larger caseous nodules were observed, with little evidence of fibrosis. At the hilum and in the lower lobe several sharply defined, caseous nodules were noted. Microscopic sections revealed an extensive tuberculous pneumonic process in the consolidated region; typical tubercles and areas of caseation were seen. The left lung was markedly edematous but there was no evidence of tuberculosis.

The liver was massive and firm, weighing 2,200 gm. The hepatic venous radicles were markedly distended. The portal and splenic veins were patent and distended. The portal vein appeared to be kinked at the hilus of the liver. The capsule of the liver was thickened irregularly and presented fibrinous deposits. On section the liver was nutmeg in appearance. Microscopically the picture was that of extensive chronic passive congestion compressing the surrounding liver tissue, with some central fibrosis and atrophy and moderate fatty changes. In some areas there was connective tissue replacement within the central portions of the lobules.

The spleen was moderately soft, weighed 550 gm. and revealed the histological picture of marked chronic passive congestion.

COMMENT

Our case presents the unusual feature of clinical portal obstruction associated with fatal intraperitoneal hemorrhage from a ruptured abdominal varix. On clinical and pathological examination there was a healed pancarditis, the etiology of which was probably rheumatic.

While active tuberculosis of the right upper lobe of recent origin was present, the findings lead us to believe that this condition had no causative relation to the adhesive pericarditis and to the condition simulating portal cirrhosis.

A clinical picture of cirrhosis of the liver and negative findings at necropsy is not uncommon in adherent pericardium, whether due to tuberculosis or to rheumatic heart disease. Friedl Pick³ and R. C. Cabot⁴ many years ago called attention to cases of long-standing pericarditis with a clinical picture of portal cirrhosis. The course was one of dyspnea, large liver, and recurrent ascites requiring repeated paracenteses, with only slight edema of the legs. At necropsy only an adherent pericardium and nutmeg liver were found. There was no evidence of portal cirrhosis histologically.

The mechanism by which chronic congestive heart failure due to adherent pericardium produced a picture of portal obstruction in our case warrants further comment. Marked chronic passive congestion of the liver occurs as a rule with increased venous pressure in the hepatic veins and failure of hepatic venous compensation in cases of (1) increased pulmonary vascular pressure following rheumatic heart disease with mitral stenosis, or long-standing hypertension and coronary artery disease, (2) extensive fibrotic pulmonary lesions or emphysema with narrowing or obliteration of a great part of the pulmonary vascular bed, (3) tricuspid valvular lesions, (4) constriction by pericardial adhesions of the inferior vena cava as it enters the pericardium, and (5) thrombosis of the hepatic veins. In long-standing congestive heart failure, dilatation of the hepatic veins is common. In tricuspid disease particularly the intrahepatic venous pressure may be enormously increased, and it is with this lesion that so-called "cardiac cirrhosis" and ascites are most commonly associated. In like manner constriction of the inferior vena cava by pericardial adhesions would throw an even greater burden on the hepatic and central veins with resultant markedly increased venous pressure in this region. According to Moschkowitz⁵ the long-standing increased venous pressure in the liver leads to phlebosclerosis of the central and hepatic veins. Connective tissue is deposited in the capillaries around the central veins. This in turn throws an additional burden on the portal venous system with, eventually, the production of ascites. Thus the mechanism is essentially that of the portal obstruction caused by portal cirrhosis. Another significant factor in our case may have been the kinking of the portal vein near the hilus of the liver, although the portal vein and its tributaries were patent.

Rohde⁶ calls attention to the activity of the diaphragm and its effect in aiding the flow of venous blood from the hepatic veins and inferior vena cava into the right auricle. He points out that adherent pericardium may hinder the activity of the diaphragm and thus be

another factor producing congestion in the inferior vena cava and the hepatic veins. Of great significance is the experimental work of Rehn,⁷ who produced varying degrees of narrowing of the inferior vena cava. Stasis in the region of the inferior vena cava resulted. The caval stenosis hindered the flow of blood to the heart and produced insufficiency of the right auricle due to inflow stasis. As a result of the congestion, degenerative processes in the liver parenchyma set in with, eventually, proliferation of connective tissue in the walls of the central and sublobular veins and obliteration of their lumina. In every case, increased peritoneal fluid resulted. No edema of the legs was observed. The azygos vein became dilated, but no hydrothorax was noted.

In our case the extensive pericardial adhesions to the diaphragm probably played a contributory rôle to that of the constriction of the inferior vena cava by pericardial adhesions, embarrassing the circulatory dynamics of the hepatic venous system and producing the clinical picture of portal obstruction.

SUMMARY

1. A case of healed rheumatic heart disease with adherent pericardium and a clinical picture of portal obstruction is reported. Death occurred from a ruptured retroperitoneal varix with hemoperitoneum. Active pulmonary tuberculosis was an incidental finding at necropsy.

2. The mechanism of so-called "cardiac cirrhosis" and its relation to the production of a picture of portal obstruction are discussed.

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ELECTROCARDIOGRAPHIC EVIDENCE OF RECENT CORONARY THROMBOSIS SUPERIMPOSED ON BUNDLE-BRANCH BLOCK RESULTING FROM PREVIOUS CORONARY DISEASE

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LITTLE has been noted or written about electrocardiographic evidence of recent coronary thrombosis superimposed on electrocardiographic evidence of previous coronary disease. Therefore it is of interest and importance that I present a clear instance of such evidence with post-mortem examination. Here a change in the T-waves (Fig. 1) was discovered a few weeks after a late coronary thrombosis superimposed upon antecedent bundle-branch block which accompanied a history of ten years of angina pectoris and of an earlier coronary thrombosis; the first myocardial infarction preceded the second by three years. I have discovered no report of this finding in the literature, nor other examples in the electrocardiographic file of the Massachusetts General Hospital.

CASE REPORT

R. A. F., male, architect, first consulted me on November 8, 1929, at the age of sixty-one years, seven years after the onset of angina pectoris on effort (high substernal oppression lasting a few minutes at a time) and five months after an attack of coronary thrombosis which occurred during a trip to the Pacific Coast. For the first three years of the angina pectoris he was not much troubled by it; then it increased in frequency and severity, and after two more years, that is, in 1927, it was associated with aching in the right arm and came with excitement and nervousness as well as on exertion. In 1928 nitroglycerin was prescribed, and this drug quickly relieved the individual attacks.

His *past history* gave a record of measles, mumps, and chickenpox in childhood, typhoid fever and pneumonia at about forty years of age, a nervous breakdown at forty-nine years, herpes zoster at fifty-eight years, and renal calculus with passing of the stone in Los Angeles in the summer of 1929.

His *habits* were good. He used little tobacco, tea or coffee, and alcohol moderately. He took regular exercise.

His *family history* disclosed the fact that his father had had angina pectoris for many years (estimated at twenty-five by the patient) before his death at the age of eighty years. His mother lived to be seventy-eight years old. A grandfather died at ninety-eight years. One brother and two sisters were alive, all troubled with "heart disease." Another sister had arthritis, and two other sisters died in youth.

Physical examination by myself on November 8, 1929, revealed a tall, well-developed and nourished man, deeply tanned and apparently the picture of health.

His breathing was normal. The pupils were equal and reacted normally to light. There was a slight arcus senilis in both eyes. The thyroid gland was not enlarged. The teeth were mostly false. The tonsils were small. There was no abnormal pulse in the neck, either arterial or venous. The heart was somewhat enlarged, with apex impulse and left border of dullness at the sixth rib, 10 cm. to the left of the mid-sternal line and just beyond the midclavicular line. There was no abnormal dullness at the base of the heart or to the right of the sternum. The heart sounds were rather poor in quality, and there was a slight protodiastolic gallop rhythm at the apex. There were no murmurs or thrills. Occasional premature beats were heard. The pulse was normal in form and the radial arteries were soft. The lungs were clear and the abdomen was normal. There was no edema over the shins. The

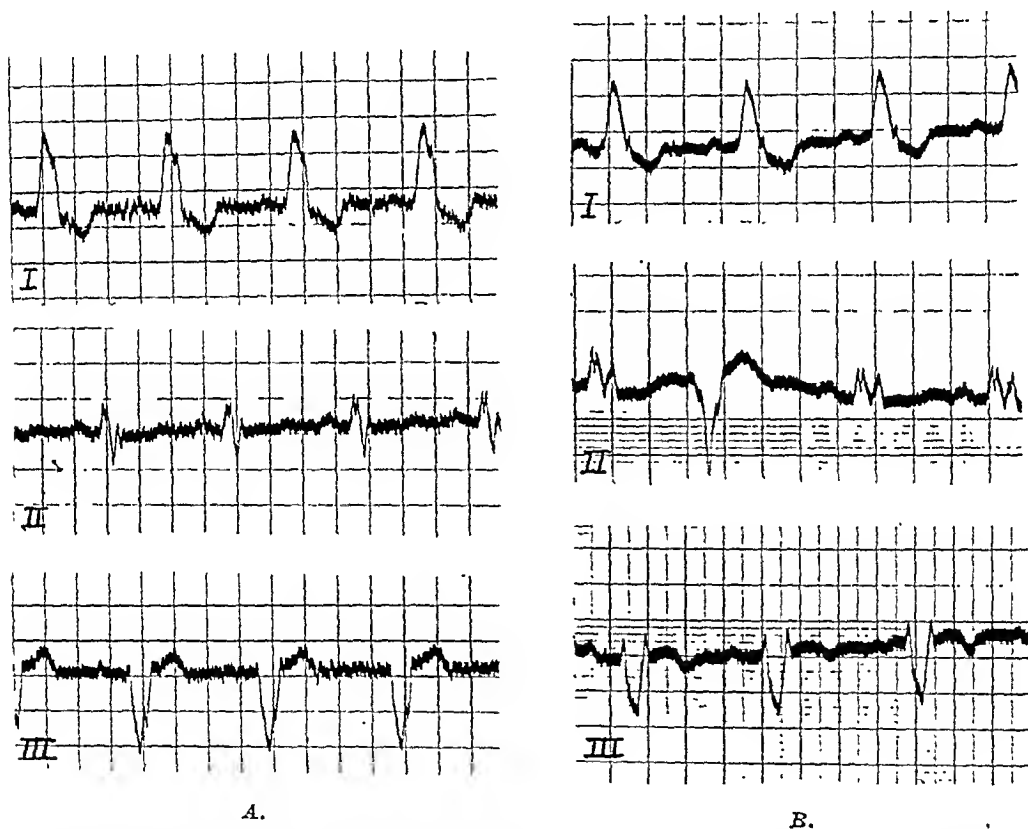


Fig. 1.—Electrocardiograms (Leads I, II and III) of patient R. A. F., first (Aug. 17, 1931), following nine years of angina pectoris and two years after a first coronary thrombosis (A); and second (Sept. 16, 1932), seven weeks after a second coronary thrombosis (B). Time = 0.2 second. Amplitude: 1 mm. = 10^{-4} volt.

Bundle-branch block with left axis deviation is evident in both records, but in the second there has developed a change in the T-wave, especially in Lead III and slight changes in the QRS-wave, most evident in Lead II.

knee jerks were normal. The pulse rate was 84 and the blood pressure was 165 mm. mercury systolic and 100 mm. diastolic with slight alternation (5 mm.).

Electrocardiograms Nov. 8, 1929, Aug. 26 and Nov. 24, 1930, May 19, Aug. 17, and Nov. 23, 1931, and Feb. 29, 1932, showed bundle-branch block with left axis deviation (Fig. 1 A) and ventricular premature beats in the 1929 record. On May 26, 1930, the bundle-branch block was temporarily absent; the electrocardiogram on that day showed normal rhythm at a heart rate of 70 with marked left axis deviation but narrow QRS waves within normal limits of duration and low but upright T-waves throughout.

Course of Illness. During the next three years and until his death I examined this man at intervals of three to six months. For these examinations he was able to come to my office except in the summer of 1932, when I saw him at home during his acute illness with coronary thrombosis.

Through the spring and summer of 1930 he improved considerably, having only occasionally a little angina pectoris if he hurried when carrying a bundle or if he became angry. He required only about 8 tablets of nitroglycerin a month. The only other medication was the use of metaphyllin or theominal at times. If he did not hurry, he was able to do a good deal without discomfort: he was busy in his work, frequently walked several miles a day, often swam, and even climbed six flights of stairs at a time. In May, 1930, not only did he show much subjective improvement, but his gallop rhythm, pulsus alternans, and even his bundle-branch block were no longer present. His blood pressure averaged about 150 mm. systolic and 90 mm. diastolic. In the winter of 1930-1931 he was not quite so well but nevertheless quite active and in a fair state of health. His bundle-branch block had returned. In the spring and summer of 1931 he again gained in health and could go sometimes for a week without requiring nitroglycerin. Through the next fall and winter he was not quite so well, cold weather and business worries apparently being responsible.

On July 23, 1932, he suffered an attack of severe substernal pain radiating down both arms and lasting altogether about eighteen hours. Morphine and codeine gave partial relief. Fever and dyspneic spells followed for a few days, and on July 27 when I saw him he showed some orthopnea, a return of his protodiastolic gallop rhythm at the cardiac apex, a reduced blood pressure (110 mm. systolic, 80 mm. diastolic), moderate engorgement of the neck veins, and slight enlargement of the liver. After digitalization and prolonged rest in bed he improved greatly and on September 16 he was able to come convalescent to my office. At that time his physical examination showed much the same findings as before the recent attack of coronary thrombosis, and there was no sign or symptom of congestive failure. Angina pectoris had returned.

On this date, September 16, 1932, his electrocardiogram was of considerable interest, showing as it did not only the bundle-branch block, as before, but a change in the T-waves, especially in Lead III (Fig. 1 B), undoubtedly the result of the new myocardial damage. There was also a slight change in the QRS waves. One ventricular premature beat was recorded in Lead II.

In October, 1932, acute congestive failure came on after undue exertion, and following a week of orthopnea and progressive failure the patient died (October 10, 1932).

Post-mortem examination showed a very large heart, weighing 800 grams, with hypertrophy and dilatation of both ventricles. The left ventricular wall measured 18 mm. in thickness except at an area of considerable thinning $2\frac{1}{2}$ cm. in diameter in the anterior wall 2 cm. from the apex and 1 cm. from the interventricular sulcus; the right ventricular wall was 8 mm. thick. Adjacent to the old scar in the anterior wall of the left ventricle at the point of thinning mentioned above there was evident softening and necrosis of the muscle in two areas—one to the left and near the apex 3 by 2 cm. in diameter and the other at the junction of the anterior wall and the interventricular septum. Overlying these two areas on the endocardium were two partly organized ante-mortem mural thrombi. There was a small firm scar in the myocardium of the left auricle near the tip of the appendage.

Coronaries: On dissection the anterior descending branch of the left coronary artery was found to bifurcate into two branches at a point 4 cm. below the main left coronary division. Continuing distally one of these branches coursed a trifle to the

left of the interventricular septum. This branch was found to be completely occluded for a distance of 2 cm. by a calcification of its wall. The second branch coursed distally toward the apex of the heart in a region about midway between the left blunt border and the interventricular septum. This vessel was found to be occluded by a definite grayish red thrombus 2.5 cm. from the point of bifurcation. These two vessels were split in a Y-shaped manner to enclose the dimpled area on the surface of the ventricle. The right coronary showed marked arteriosclerotic changes with slight diminution in the lumen, but at no place was it completely occluded. The left circumflex coronary branch was comparatively free from arteriosclerotic changes. The orifices of both the right and the left coronaries were completely surrounded by atheromatous plaques, and their mouths were diminished in size, measuring approximately 3 mm. in diameter. The ascending thoracic aorta was somewhat atheromatous but showed very little calcification. The valves showed no abnormalities except for slight atherosclerosis.

SUMMARY

A case is reported of electrocardiographic evidence of recent coronary thrombosis, chiefly a change in the T-wave of Lead III consisting of a late inversion, superimposed on bundle-branch block from previous coronary disease in a man who died at the age of sixty-four years, ten years after the onset of angina pectoris, three years after his first coronary thrombosis, and three months after his second coronary thrombosis. The bundle-branch block was found a few months after the first myocardial infarction, and the new T-wave change a few weeks after the second.

CALCIFICATION OF THE MYOCARDIUM FOLLOWING CORONARY OCCLUSION

A CASE REPORT

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DIAMOND¹ in reviewing the literature on myocardial calcification discovered forty-four recorded instances.

These cases were divided into three groups, due respectively to vascular disease in the heart, to some infection, or to toxic causes. The condition follows necrosis or certain forms of degeneration, excepting fatty degeneration. Of those due to vascular disease the first instance of myocardial calcification obviously due to coronary disease was reported in 1768 by Bordenave.² Ten others due to vascular disease in the heart muscle have been reported since. That described by Scholz³ most nearly approximates the findings as appended in this case report.

CASE HISTORY

Patient A. L., aged sixty years, male, laborer, first seen July 12, 1933, by Dr. K. W. Emanuel of Duluth.

Present Complaint: Numbness of the left foot.

History of Present Illness: The patient stated that the present illness began June 23, 1933, when he contracted what he thought was the "flu." He had a nasal discharge with some sneezing, felt tired, and had general aches and pains throughout his body. On July 5, 1933, he saw a physician, who advised him to go to bed and who told him he had heart trouble. The specific data of the diagnosis, however, are wanting. On July 11, 1933, his left large toe suddenly became cold, and within half an hour this numb and cold sensation had extended as far as his knee. He entered the hospital on July 12. On inquiry it was found that the patient had always felt well except for some slight dyspnea on exertion which he had observed occasionally for several years.

Past Medical History: In 1916 the patient was told that he had heart trouble, although he never had any symptoms that appeared to be referable to his heart. However, he was sick in bed for two weeks at that time and was thought to have influenza. This history might have some bearing on the autopsy findings in this case, and may have indicated a disability incident to a coronary occlusion.

Social History: Married, no children. Denies ever having had any venereal disease. Family history negative.

Physical Examination: The patient was well developed and nourished and appeared to be about sixty years of age. Color and strength appeared normal. Mental cooperation was excellent.

The examination of the head and neck, including special sense organs, was negative except for several carious teeth.

The examination of the chest indicated a moderate enlargement of the heart and an irregular rhythm probably due to an auricular fibrillation, but gave no other abnormal evidences. The lungs were negative.

The pulse rate was 100 per minute and irregular. The blood pressure was 133/90.

Extremities: The left foot and leg up to a point below the left knee were cold, bluish in color and mottled. The knee reflexes were absent on the left side, and there was an inability to move the left foot or ankle. Sensation was absent in the left foot and leg to a point 1 inch below the knee.

A diagnosis was made of gangrene of the left leg, probably associated with his myocardial insufficiency and auricular fibrillation. The obstruction to the circulation was probably due to an arterial embolus incident to intramural cardiac thrombi.

On July 14, 1933, the left leg was amputated below the knee by Dr. E. E. Webber, and the immediate postoperative convalescence was characterized by no adverse developments.

The gangrene appeared to continue up the left thigh, and on July 23 it was found necessary to disarticulate the left leg at the hip. It was found that all the large vessels, arterial and venous, were thrombosed. The patient's condition remained good, and his wound healed satisfactorily.

On September 11, 1933, the patient became stuporous and developed a paralysis of the entire left side of the body. He finally lapsed into coma, and died September 16, 1933.

The diagnosis of the condition immediately preceding his death was that of a cerebral embolism in the right hemisphere.

Autopsy Findings: Upon opening the thoracic cavity there were extensive and tough fibrous adhesions over the left upper lobe and between the lower lobe, left, and the diaphragm. The right lung showed a few fibrous adhesions to the diaphragm. Upon opening the pericardium the anterior surface of the left ventricle was found attached by tough fibrous adhesions to the anterior wall of the pericardial sac. The adherent part of the left ventricle showed extensive calcification. The heart contained some clotted blood and the left ventricle small masses of mural thrombi. The anterior part of the left ventricle bulged forward, quite thin and densely calcified in an area measuring about 7.5 by 6.5 cm. This area, which was quite rigid, had the shape of half of the shell of an egg, its concavity forming part of the internal surface of the left ventricular septum. The left ventricle and the left auricle were somewhat dilated. The mitral valves showed a very cloudy yellowish area, the aortic valves slightly thickened and sufficient. The coronary arteries showed marked arteriosclerotic changes, and the anterior descending branch of the left coronary was partly obliterated. The heart weighed 480 gm. The left lung weighed 600 gm., the right lung 500 gm. Both apices showed fibrous areas. Both lungs revealed areas of bronchopneumonia in their posterior and lower parts. There was a small embolus in the left lower branch of the pulmonary artery and a large embolus in the main branch of the right pulmonary artery. In the right lower lobe was a large hemorrhagic infarct. The bronchi were somewhat diffusely dilated and contained much seromucous purulent material. Their mucosa was quite congested. The hilus glands showed nothing of note.

The spleen weighed 130 gm., with several old and more recent anemic infarcts. The adrenals indicated nothing of note. The capsule of the kidneys was adherent in places. The kidneys weighed 280 gm. and showed several old and more recent anemic infarcts. The liver weighed 1,330 gm. and showed marked chronic congestion. The remaining abdominal organs showed nothing

of importance. The left external iliac artery was thrombosed up to the point of bifurcation of the left common iliac artery. The left iliac vein was thrombosed. The aorta showed arteriosclerosis Grade II.

Upon opening the skull, the dura was somewhat adherent to the internal surface of the skull. The internal surface of the dura was smooth. The sinuses of the dura contained partly clotted blood. The convolutions of the brain were somewhat flattened, and there was but little subarachnoidal fluid. The arteries of the base of the brain showed a few quite small yellowish spots. The right middle cerebral artery was closed by a small embolus and a massive thrombus. The ventricles of the brain contained some slightly bloody fluid. There was a large area of softening of the right cerebral hemisphere, involving mainly the right temporal lobe and extending to the lenticular nucleus and the internal

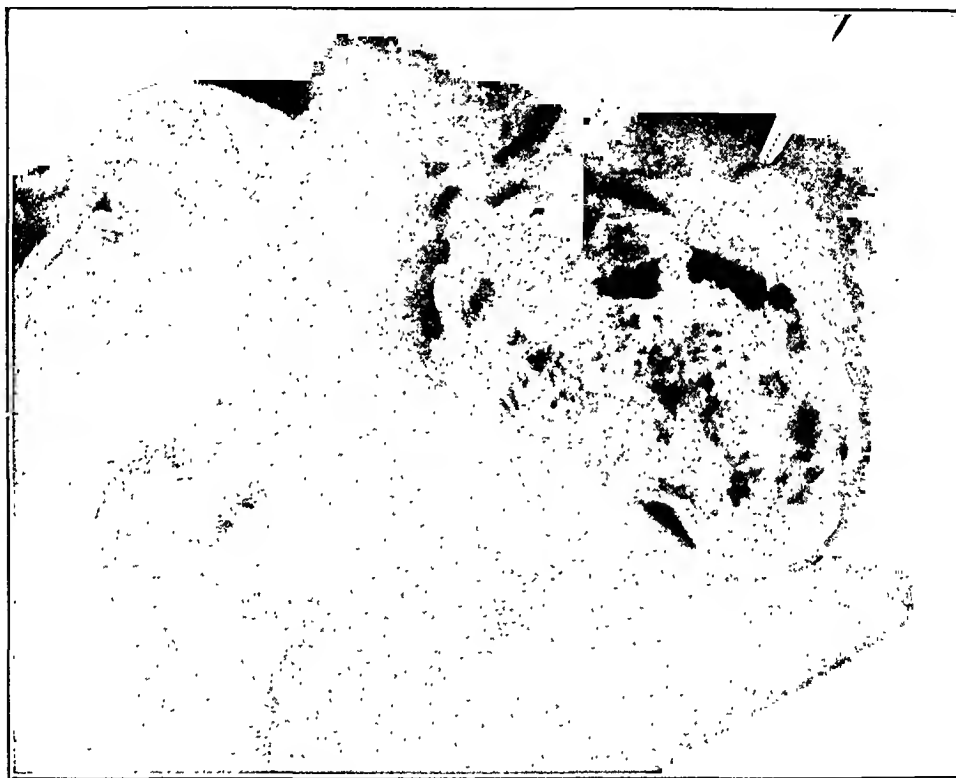


Fig. 1.—Roentgenogram of heart taken post mortem, illustrating plaque calcification of left ventricle.

capsule. The left cerebellar hemisphere showed also a large area of softening which involved about four-fifths of the lobe.

The roentgenogram shown in Fig. 1 indicates clearly the degree of density and the extent of the calcified plaque in the left ventricle.

Microscopic Examination.—Sections have been made after decalcification through the densely calcified areas of the wall of the left ventricle. Those areas are formed by masses of fibrous connective tissue with only a few cellular elements. In the calcified areas the nuclei cannot be recognized. The tissue is hyaline and densely infiltrated with lime salts. A few bundles of muscle fibers which are embedded in the fibrous areas surrounding the calcified parts are atrophied and show a definite increase of the interstitial connective tissue. In some areas the tissue is infiltrated with a few scattered lymphatic cells.

SUMMARY

An instance of myocardial calcification subsequent to coronary occlusion is reported in which the plaquelike calcification involves the area of the heart muscle supplied normally by the occluded descending branch of the left coronary artery.

REFERENCES

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Society Transactions

NEW YORK COMMITTEE ON CARDIAC CLINICS, 1934

THE annual scientific meeting of the New York Committee on Cardiac Clinics was held in New York City on April 24, 1934, with Doctor J. Hamilton Crawford as presiding officer.

The following are abstracts of papers presented or read by title:

Fibers of the Purkinje System in the Walls of the Mammalian Ventricle. David I. Abramson, M.D.

ABSTRACT

It is generally considered that the impulse in the heart, after spreading over the subendocardial Purkinje system, leaves this network to extend throughout the ventricular musculature by virtue of the conductivity of the myocardium itself. However, a study of beef, sheep and pig hearts by means of the injection method shows that these hearts contain, besides the subendocardial Purkinje network, another set of Purkinje fibers which penetrates the ventricular musculature. These myocardial fibers extend practically throughout the outer walls of both ventricles, reaching in many sites as far as the epicardium. They form plexuses and ramifications similar to the subendocardial network, of which they are a continuation. In the outer wall of the left ventricle these myocardial plexuses are disposed in layers which extend roughly perpendicular to the subendocardial network; whereas in the outer wall of the right, the layers are nearly parallel to the subendocardial network and to one another. In the interventricular septum, myocardial Purkinje fibers are also present, connecting the subendocardial network of the right ventricle with that of the left. Employing special staining methods, histological studies were made which confirmed the results obtained by injection and also demonstrated that in structure and staining properties these myocardial fibers are similar to the subendocardial Purkinje plexus.

Growth of the Cardiac Silhouette and the Thoraco-abdominal Cavity During Infancy. The Influence of Undernutrition. Harry Bakwin and Ruth Morris Bakwin.

ABSTRACT

At birth the cardiac silhouette lies anterior to the fifth to the tenth dorsal vertebrae. It is globular and more centrally placed than it is later in life. The left cardiac outline is ordinarily convex and only rarely shows the divisions seen in later life. During the first year the heart grows rapidly, the frontal plane doubling its area. At the end of the first year the heart silhouette is less horizontal than at birth. The left border often shows the divisions seen in later life, at times very prominently. Averages and standard deviations for the dimensions by certain subdivisions of age under one year were calculated. The transverse diameter of the cardiac silhouette is poorly correlated with total body length, body weight, sitting height, biacromial diameter, bimalar diameter. There is a low correlation with the thoracic width, measured roentgenologically. The growth in size and shape of the cardiac silhouette in the healthy group was compared with that in a group of undernourished infants. In the latter the cardiac silhouette grows more slowly than in

healthy infants. The retardation in growth of the heart is greater than that of total body length or thoracic width so that the heart becomes smaller, relative to total body length and to thoracic width, than is the case in normal infants.

Results of Intensive Ambulatory Treatment of Advanced Cardiac Insufficiency. Meyer Friedenson, M.D.

ABSTRACT

Ambulatory treatment was applied to cases of advanced cardiac insufficiency over a period of several years. These individuals had hitherto required numerous hospital admissions. We were guided chiefly by the weight, degree of dyspnea, and ventricular rate. The chief problem was the control of fluid accumulation. Treatment consisted mainly of intensive use of diuretic measures. Fluid and salt intake was restricted by calculated diets. "Maintenance diuretics," urea or ammonium nitrate, were given constantly to help prevent fluid reaccumulation. Frequent injections of salyrgan were used when rapid action was necessary. Digitalis and other drugs were administered when indicated. Through special arrangement the patient was treated at home if temporarily unable to attend the clinic. The fact that the patients can remain at home is of distinct psychological importance. It is not claimed that improvement thus obtained renders the patients less liable to sudden death. Whether life has actually been prolonged, we cannot say. There is no doubt, however, that existence is made much more tolerable. Intensive ambulatory treatment with diuretic measures affords considerable relief for prolonged periods to many patients who do not respond to the usual methods.

The Effect of Edema on the Amplitude of the Electrocardiographic Waves. Morris Goodman, M.D.

ABSTRACT

The object of this study was to determine whether edema is a factor in the production of low amplitude of the electrocardiographic waves of patients who have advanced heart disease. (1) Three dogs were made markedly edematous by the method of plasmaphoresis. Electrocardiograms were taken before, during, and after edema. The amplitude of the waves of Leads II and III in each instance fell to about one-third the original height. The waves of Lead I remained unchanged or fell slightly. When the edema disappeared, the amplitudes increased. (2) In seven animals localized edema was produced about the chest by infiltrating saline under the skin of that area. Electrocardiograms were taken before, during, and after infiltration was absorbed. The results were similar to those observed when generalized edema was produced. (3) In four animals 1,000 c.c. of saline were infiltrated into the thighs. In no instance was a fall in amplitude of the electrocardiographic waves produced. (4) In six patients 1,000 c.c. of saline were infiltrated into the chest wall. The amplitude of the electrocardiographic waves showed little or no effect when conventional leads were used but showed a consistent fall with chest leads. Electrocardiograms of 27 patients were studied. These patients while under care lost a minimum of 6 kilograms of weight, representing edema fluid. Only 5 showed a consistent increase in amplitude as the edema disappeared. The increase to maximum amplitude occurred before all the edema disappeared. The loss of weight in this group was in excess of 12 kilograms. There were others with an equal loss of weight who showed no change. Conclusions: (1) Edema fluid in the tissue close to the heart causes a decrease in the amplitude of the electrocardiographic waves when the edema is of large and sufficient quantity. If the edema is localized, it will decrease the amplitude of the waves obtained by leading off from the site of edematous tissue. (2) The edema need not be in the cardiac musculature. (3)

The amount of edema generally seen in patients with congestive heart failure has little or no effect on the amplitude of the electrocardiographic waves because it is rare to have it distributed to as high a level as the chest wall.

Studies on the Myocardial Aschoff Body. Louis Gross, M.D., and Joseph C. Ehrlich, M.D.

ABSTRACT

The clinical histories and anatomical material from seventy cases of uncomplicated rheumatic fever with Aschoff bodies in the myocardium were investigated. A histological classification of the Aschoff body is suggested. This classification includes seven types of lesions which apparently bear some relation to the life cycles of the Aschoff body. It is shown that these lesions pass through three phases. The earliest phases have been found to occur up to the fourth week after the onset of the illness; the middle phases, between the fourth and thirteenth week, and the late phases from the ninth to the sixteenth week. The earliest types of specific lesions occur in two forms. As a consequence, the evolution of the lesions may take one of two courses, determined by the initial lesion.

Some Observations Concerning the Use of Mercurials in Heart Disease. Robert H. Halsey, M.D.

ABSTRACT

When the edema and anasarca of heart failure do not respond to digitalis and theophyllin therapy, preparations of salts of mercury may cause a diuresis and complete relief. The mercury salts vary in content and are said to contain 33.9, 39.6, and 41.1 per cent of mercury. Some preparations have a maximum and minimum percentage prescribed: "not less than 38.0 per cent nor more than 41.0 per cent when calculated to the dried substance." Intravenous administration may produce a diuresis the amount of which will vary with the fluid intake. The repeated use of the preparation at short intervals may be associated with a decreasing output. A rest period of several days may be followed by another period of large output succeeded by a day-to-day decreasing output. Any one of the mercury preparations responds in this way—the relation of the size of the dose, or the mercury content to this variable output is not clear. It does not appear to be a response regularly proportionate to the mercury percentage of the preparation administered. One-half c.c. at one period may cause as profuse a diuresis as 2 c.c. of the same preparation. Elements of irritation, stimulation, and fatigue are apparently uncertain variables.

Trans-Thoracic Electrocardiography; Clinical Use of the 9-Lead Hook-Up. (Lantern Slides.) Albert S. Hyman, M.D.

ABSTRACT

The conventional three-lead method of electrocardiographic study fails to reveal cardiovascular pathology in 18 per cent of cases which post-mortem show extensive disease. The explanation lies in the fact that the original electrodynamic triangle of Einthoven conceives the heart in situ as a triangular plane. Lesions outside this mathematical formula fail to register. The original work of Waller with his 16 leads is reviewed. The heart is conceived as a solid organ represented as a triangular plane turned on a vertical axis and thus producing a cone. The 9 divisions of the electrodynamic cone and their electrical mathematical formulae. The clinical use of the trans-thoracic leads. Description of the leads and the electrodynamic segments of the cone displayed. Demonstration of the 9-lead electrocardiographic hook-up. Normal records from birth to old age. Clinical histories of patients with un-

questioned cardiovascular disease but with normal three conventional lead electrocardiograms. Reexamination of these same cases by the 9-lead hook-up. The Witkin formula for the localization of coronary infarcts, with illustrative cases showing 9-lead records and post-mortem specimens. Statistical data in regard to prognosis from localization.

Convalescent Care of the Cardiac Child. Alexander T. Martin, M.D.

ABSTRACT

Analysis of 963 cardiac children ranging from six to sixteen years at three convalescent homes (Martine Farm, Reed Farm, and Nichols Cottage) near New York City. Study covers thirteen years and comprises 1,279 visits. Children were drawn from 54 institutions or agencies in Greater New York. Two hundred fifty-three or 26.2 per cent of these children have died, death being due in the majority of cases to a reactivation of the rheumatic state with carditis. Seven hundred and ten or 73.8 per cent are living. Average stay 152 days. Average gain in weight 6.1 pounds. Etiological study shows 74.5 per cent to have had rheumatism. This includes polyarthritides and chorea. Congenital heart disease 3.5 per cent. Cases studied are Groups IIA and IIB. Return visits show an increasing number in the IIB group. Value of tonsillectomy inconclusive. Active follow-up maintained in the 710 living children, 45.4 per cent through cardiac clinics and 19.1 per cent through correspondence and home visits. Of the latter group 53.5 per cent under no medical supervision. Of 18 girls married, 5 have no children, 11 have one child, and 2 have two children. One of these died following cesarean section. Figures on incidence of rheumatic reactivation following return from the convalescent home are not conclusive because reliable criteria are not available in most cases.

The Two-Step Test of Myocardial Function. Arthur M. Master, M.D. To be published.

Ergotamine Tartrate in Paroxysmal Auricular Tachycardia. Charles J. Oppenheim, M.D.

ABSTRACT

The various methods generally employed to secure an abatement of attacks of this troublesome condition indicate how ineffectual any one method has proved to be. Based upon the experimental studies showing that ergotamine tartrate has a depressing effect upon both augmentor and inhibitor sympathetic fibers, and tends to produce marked slowing of the heart rate, it has been given to patients during attacks, hypodermatically in doses of 0.0005 gm. In one case it was possible to obtain electrocardiograms during and immediately following cessation of the attack. In practically all cases cessation of the attack has been striking, prompt, and without apparent ill effect. It would appear that ergotamine tartrate is a valuable drug in the treatment of attacks of paroxysmal tachycardia.

The Size of the Angle of Clearance of the Left Ventricle as a Criterion of Ventricular Enlargement. May G. Wilson, M.D.

ABSTRACT

Roentgenographic observations of 504 children between the ages of five and fifteen years were made. The series included normal children and subjects with possible, potential, and organic heart disease. Teleoradioscopy at a distance of two meters and fluoroscopic examination in the three standard positions, namely, posterior

anterior, left anterior, and right anterior oblique was made on each subject. Standard degrees of rotation were used in the oblique positions. This is a simple, reasonably accurate roentgenographic method for recognizing cardiac abnormality in children. The *angle of clearance* of the *left ventricle* in the left anterior oblique position differentiated with the greatest degree of frequency the normal from the abnormal heart, compared with measurements of the frontal plane of the cardiac silhouette. A normal *angle of clearance* of the left ventricle (of less than 55 degrees) in the left anterior oblique position would seem to be a reliable radiological criterion.

The Effect of Continuous Infusions of Minute Doses of Epinephrine on the Blood Pressure, Urea Excretion and Urine Volume in Various Clinical Conditions Including Bright's Disease. Charles A. Poindexter, M.D., and Herman O. Mosenthal, M.D.

ABSTRACT

Richards observed that minute doses of epinephrine brought about a constriction of the efferent vessel of the glomerulus and a dilation of the afferent vessel and resulted in a definite increase in urinary secretion (frog). This observation was the stimulus for this experimental work because it was thought that its application might be of value in the treatment of uremia. By means of a Woodyatt continuous infusion apparatus epinephrine was given intravenously in doses of approximately 0.0005 mg. per kilogram per minute. In two moribund patients with low arterial tension the injection of epinephrine resulted in an elevation of the blood pressure which was directly proportional to the dose of epinephrine and which was maintained during the period of the infusion. In patients with a normal or an initial elevated blood pressure (Bright's disease) there is no notable rise of blood pressure with the amounts of epinephrine employed. The urea concentration in the urine usually increased during the period of injection. The urine volume usually increased both during and several hours following the continuous infusion of epinephrine. No harmful effects were observed in any of the patients.

The Action of Quinine and Quinidine on Patients With Transient Ventricular Fibrillation. Sidney P. Schwartz, M.D., and Abraham Jezer, M.D. (See AMERICAN HEART J. 9: 792, 1934.)

Studies on Transient Ventricular Fibrillation. IV. The Post-Fibrillatory Period: A Definite Clinical Entity. Sidney P. Schwartz, M.D., and Abraham Jezer, M.D.

ABSTRACT

Clinical and electrocardiographic studies were carried out on four patients with auriculoventricular dissociation subject to transient seizures of ventricular fibrillation. Many observations have revealed that the period immediately following a seizure of syncope due to transient ventricular fibrillation is of a definite pattern. When fibrillation of the ventricles ceases, the recovery process to normal is characterized by a progressive increase of the idioventricular rate from 6-12 beats per minute to as high as 160 beats per minute before there is a return to the basic rhythm. This is characteristic of syncopal seizures associated only with transient ventricular fibrillation. In all other types of syncopal seizures, such as those associated with standstill of the ventricles, the return to normal rhythm is totally different. The existence of transient ventricular fibrillation as responsible for a syncopal seizure may be suspected in a patient if, following the period of syncope, the ventricular rate is found to have increased far above that of the basic level.

Department of Reviews and Abstracts

Selected Abstracts

Sager, Robert V., and Sohval, Arthur S.: Combined Syphilitic and Rheumatic Disease of the Aortic Valve. *Arch. Path.* 17: 729, 1934.

Three cases of combined syphilitic and rheumatic disease of the aortic valve are reported. In the presence of commissural syphilis, sclerotic deformities of the aortic valve usually occur. When rheumatic lesions are found elsewhere in the heart, it is at times impossible to decide from macroscopic examination alone whether rheumatic disease participated in the production of the aortic valvular defect. By the aid of established histologic criteria for the recognition of rheumatic and syphilitic disease of the aortic valve it is possible to demonstrate such participation, if it exists. Emphasis is placed on the limitation of syphilitic changes in the aortic leaflets to their commissural extremities in the great majority of cases and on the diffuse nature of the characteristic lesions of rheumatic valvulitis. Interstitial valvulitis in the midportion of an aortic cusp, particularly with fibroelastic vascularized reduplications on the ventricular aspect, usually signifies disease other than syphilis (nearly always a rheumatic infection). Association of these two types of histopathological lesions establishes the existence of combined syphilitic and rheumatic disease in the aortic valve. The rarity of this association is indicated by the fact that it has, to the author's knowledge, never been previously reported.

McGinn, Sylvester, and White, Paul D.: Clinical Observations on Aortic Stenosis. *Am. J. M. Sc.* 188: 1, 1934.

A study of aortic stenosis is presented based on 123 cases proved at postmortem examination among 6,800 necropsies of patients with all types of disease at the Massachusetts General Hospital and 113 clinical cases among 4,800 patients studied in cardiovascular consultation practice. In the post mortem series 71 per cent of the patients were males and in the clinical series 63 per cent.

Aortic stenosis occurred in the postmortem series almost as often as did mitral stenosis. The lower incidence in the clinical series may be due in part to the fact that it is difficult or impossible clinically to diagnose aortic stenosis if the stenosis is but slight in degree. Closer search for the lesion resulted in the finding clinically of twice as many cases of aortic stenosis, definite or questionable, in the second half of the clinical series as in the first half. It appears justifiable to make the clinical diagnosis of aortic stenosis when a loud harsh systolic murmur is heard in the region of the second right intercostal space and is transmitted to the neck, in the absence of pronounced aortic dilatation due to luetic aortitis or marked hypertension, especially when there is evidence of other valvular deformity or a history of rheumatic infection. An aortic systolic thrill, a diminished or absent second aortic sound, a plateau pulse, and an aortic diastolic murmur are important confirmatory findings; but it is not necessary to await the presence of all these signs before making the diagnosis. If one waits for all these signs, a large majority of cases of aortic stenosis often of considerable clinical importance would be missed.

A comparison has been made in the postmortem series, of cases showing calcareous changes in the stenosed aortic valve with cases showing no calcareous change in the valve. Calcareous valvular changes were found more frequently than non-calcareous (86 to 37) with males predominating and living past middle life in the calcareous group while the sexes were evenly distributed in the noncalcareous group, few of whom lived longer than fifty years. Angina pectoris, cardiac asthma and higher blood pressures were more frequently found in the calcareous group, while a positive rheumatic history and auricular fibrillation were more frequent in the non-calcareous group. The average pulse pressures were approximately the same. The heart weights were similar in the two groups, but calcareous changes in the mitral valve, aorta and coronary arteries were much more common, as would be expected, in the older, calcareous group. The presence or absence of calcareous changes in the aortic cusps is clinically relatively unimportant as compared to the aortic stenosis itself, excepting as it alters the degree of stenosis or aids in the roentgen ray diagnosis.

A comparison of the autopsied cases having aortic stenosis alone with those having aortic stenosis combined with mitral stenosis showed males to be represented equally in both groups; females, however, were three times more frequent in the combined than in the isolated group. Mitral stenosis was found much more often in the patients dying under fifty years, while aortic stenosis alone occurred most commonly in people beyond that age. Angina pectoris was found more often in patients with aortic stenosis alone (14 to 2), while auricular fibrillation occurred much more often in cases with complicating mitral stenosis (26 to 13). The average heart weights were approximately the same for the two groups (612 gm. and 592 gm.). Coronary sclerosis and aortic sclerosis were more common in cases of aortic stenosis alone; sclerotic changes in the mitral valve were found in 23 of the 50 cases with complicating mitral stenosis.

In three groups of patients of the postmortem series having various degrees of calcareous aortic stenosis, it was found that the correct diagnosis had not been made clinically in any having only moderate calcareous changes, mostly at the base of the aortic cusps, and that the symptoms of congestive failure were less frequent in this group than in those instances where the lesion was more marked. At least a few of the cases showing only moderate aortic stenosis should have been diagnosed correctly antemortem if proper attention had been directed to the signs that were present. The patients with pronounced aortic insufficiency in addition to aortic stenosis had a shorter terminal illness and died at a younger age than did the patients in whom stenosis of the valve predominated. The average weight of the hearts in the group with pronounced aortic insufficiency was also higher, the smallest hearts being found in those cases with little or no aortic insufficiency and with only a moderate amount of stenosis.

It is evident from this analysis that all grades of aortic stenosis exist, much as in the case of mitral stenosis; that aortic stenosis even of considerable degree is common, particularly in males; that it is doubtless often caused by infection, especially rheumatism; that calcareous changes are found chiefly in the older patients, no matter what the cause; that aortic stenosis is less serious than aortic regurgitation of high degree, being found in many old patients after years of valvular disease; that it is sometimes associated with considerable hypertension; that, as in the case of mitral stenosis, the symptoms and signs vary in number and degree with the extent of the aortic stenosis; that aortic stenosis is often overlooked when it should be clinically diagnosed; and that it is an important lesion to search for, even in the lesser grades because of the progression of the lesion and of the frequency with which it is associated with congestive heart failure.

Greenspan, Edward B.: Carcinomatous Endarteritis of the Pulmonary Vessels Resulting in Failure of the Right Ventricle. *Arch. Int. Med.* 54: 625, 1934.

Four cases of carcinomatous lymphangitis are reported, three secondary to scirrhus adenocarcinoma of the stomach and one to adenocarcinoma of the sigmoid. The cases presented all or part of the pulmonary symptoms of cough, shortness of breath, and cyanosis with inconspicuous physical signs in the lungs. The three cases secondary to scirrhus carcinoma of the stomach presented diffuse obliterative endarteritis of many pulmonary arterioles and small arteries. The widespread obliterative endarteritis of the lung was due chiefly to the influence of the carcinomatous lymphangitis of the neighboring perivascular lymphatics, rarely to carcinoma cell emboli. In two of the cases, right ventricular cardiac failure was the direct result of the diffuse obliterative endarteritis of the pulmonary vessels.

In cases of right ventricular cardiac failure presenting no significant pulmonary or cardiac findings, the possibility of a diffuse secondary carcinomatous lymphangitis of the lungs with accompanying obliterative endarteritis of the pulmonary vessels should be considered.

Craig, Winchell McK., and Brown, George E.: Unilateral and Bilateral Resection of the Major and Minor Splanchnic Nerves. *Arch. Int. Med.* 54: 577, 1934.

Five patients with essential hypertension of varying degrees of severity have been subjected to unilateral or bilateral resection of the splanchnic nerves and to removal of the first lumbar ganglion. In two subjects, significant quantitative reduction of the pressor reactions to cold resulted. In one subject, subjective and objective improvement was striking. In the most severe forms of essential hypertension, with early renal involvement and advanced organic changes in the arterioles, the effects on the blood pressure have not been striking. Resection of the splanchnic nerves is a relatively safe operation and carries small risk. No untoward effects have been noted. Further application of this surgical procedure is justifiable in the early stages of the severe progressive form of essential hypertension in young persons.

Bellet, Samuel, Johnston, Charles G., and Scheeter, A.: Effect of Cardiac Infarction on the Tolerance of Dogs to Digitalis. *Arch. Int. Med.* 54: 509, 1934.

Tolerance of dogs to digitalis was determined at various intervals of time after ligation of the coronary artery: one-half hour after ligation of the coronary artery; four days later, during the stage of acute and subacute infarction; and from six weeks to six months later, during the stage of chronic infarction. The tolerance of these animals was compared with that of animals in a normal control series.

Dogs standardized within one-half hour after ligation showed no diminution in tolerance to digitalis as compared with those in a control group. During the stage from acute to subacute infarction, there was a diminished tolerance to digitalis which averaged from 20 to 30 per cent below the average of the figures for the normal controls. In the animals with chronic infarction in which the area of infarction was considerably smaller than in the acute or subacute stage, standardized from six weeks to six months after ligation of the coronary artery, the tolerance was less than that of the normal animals but higher than that of the group with the subacute infarctions.

The diminution in tolerance after ligation of the coronary artery apparently depends on the presence of infarction and probably also on the extent and stage of the infarcted area. These findings lend support to the clinical impression that

digitalis in massive doses may be dangerous during the stage of subacute and chronic infarction and that it should be used with caution in such cases.

Lombardini, R. Velasco, and Duomarco, J.: *The Technic of Exteriorization and Suspension of the Heart in the Dog*. *Rev. Argentina de Card.* 1: 138, 1934.

A comparatively simple procedure is described to lead the action current of the heart from different extents of cardiac surface. If a dog under anesthesin is prepared in such a way as to have the heart in a hanging position, the latter can be immersed to any desired degree in a glass filled with saline solution. The action current of the heart may now be led off by two electrodes, one of them placed on the back of the animal and the other plunging in the same glass as the heart.

Using this procedure it was found that as the surface of the heart in contact with the liquid increases, the electrical variations recorded become smaller. This fact may explain the low voltage of the deflections recorded in pericardial effusion: the liquid around the heart establishes a sort of short circuit to the heart currents, and the galvanometer is not influenced by the total electrical variations.

In order to lead off the heart currents, the heart must be surrounded by elements of unequal resistance, the electrical variations following the path of the lower resistance, probably through the base of the heart and perhaps also through the part of the heart laying on the diaphragm. This might be of importance to decide the type of ventricular preponderance shown by the electrocardiogram.

Battro A., Menendez, E. Braun, and Orias, O.: *Gallop Rhythm*. *Rev. Argentina de Card.* 1: 117, 1934.

Twenty-two cases of clearly audible gallop rhythm were graphically analyzed by simultaneously recording the heart sounds and the venous pulse. In three cases the extra sound occurred during the final moments of the rapid inflow phase; in four cases the extra sound occurred during auricular contraction; in the remaining cases, the extra sound occupied a position which was coincident with both these moments, brought closer together by the increased heart rate. In the cases corresponding to the latter group, two alternatives happened: in some cases a brief interval could be observed between the two sounds; in others, on account of a perfect coincidence of both moments, there was only one sound.

Phonocardiograms taken from normal persons often show sound vibrations during the latter part of the rapid diastolic inflow (the so-called third physiological heart sound) and also, occasionally, during auricular systole (auricular physiological sound). On account of their properties, these sounds are easier to record (if adequate devices are used) than to be heard by simple auscultation.

The conclusion may be drawn that gallop rhythm results from the pathological exaggeration of phenomena hardly audible, which, however, can be more or less easily recorded in many normal individuals.

According to their mechanism of production, the following nomenclature is suggested: rapid inflow gallop, presystolic gallop and summation gallop. Summation may be either complete or incomplete.

It is impossible by simple auscultation, to ascribe any case of gallop rhythm to any particular type. The occurrence of the extra sound during the beginning, middle or end of diastole does not necessarily imply that the gallop is one of rapid inflow, summation, or presystolic, respectively. It is the graphic analysis by means of the phonocardiogram and the phlebogram optically recorded which will precisely determine the type of gallop concerned in each particular case.

Menendez, E. Braun, and Orias, O.: Phonocardiographic Studies in the Young Adult Heart. *Rev. Argentina de Card.* 1: 101, 1934.

By optically recording the heart sounds, it is possible to recognize normal acoustic phenomena which are not easily heard by simple auscultation. The third normal heart sound was neatly recognizable in 42 out of 100 phonocardiograms recorded in as many healthy medical students from twenty to twenty-five years old. Small vibrations, considered as a vestigial third heart sound, were plainly visible in 18 other records. An evident auricular sound was recorded in 15 cases, and in 5 other instances there were clear vestiges of it.

The third heart sound invariably occurs during the last moments of the ventricular inflow phase. The physiological auricular sound starts about 0.04 second after the beginning of the auricular systole.

It is probable that both, third heart sound and physiological auricular sound, have a similar mechanism of production; they might be due to the vibrations set up in the ventricular wall by the sudden inrush of the blood coming from the auricles.

Castro, Olyntho de: Partial Flutter and Fibrillation. *Arq. brasil. de cardiol. e hemat.* 1: 129, 1934.

The author suggests the term "partial flutter and fibrillation" for those cases in which tracings show an imperfect function of auricular contraction. He believes that the cause of these modifications is a partial affection of the auricular myocardium, i.e., there are certain groups of fibers which have been affected by the process resulting in flutter or fibrillation. The persistence of the P-wave although more or less altered is explained on the basis of the marked contraction of the majority of the sound fibers which give a normal sinus rhythm.

Marble, Alexander; Field, Madeleine E.; Drinker, Cecil K.; and Smith, Rachel M.: The Permeability of the Blood Capillaries to Lipoids. *Am. J. Physiol.* 109: 467, 1934.

The peripheral (cervical) lymph of normal fasting dogs contained on the average per 100 c.c. of lymph the following: cholesterol, 56 mg.; fatty acid, 239 mg.; and total lipid, 305 mg. These values are respectively 41 per cent, 54 per cent, and 52 per cent of those for cholesterol, fatty acid, and total lipid in blood plasma from the same dogs. Blood and lymph samples were obtained as nearly simultaneously as possible.

Following the intravenous injection of fat-laden chyle or of a fat emulsion, there usually occurred within one to four hours a slight rise in the total lipid content of the cervical lymph. Under such conditions no significant change occurred in the cholesterol content of the lymph despite the production at times of a mild hypercholesterinemia.

These experiments suggest that the degree of permeability of the blood capillary wall to lipid substances other than cholesterol is slight but definite and is greater than that to cholesterol itself.

Himwich, H. E., Goldfarb, W., and Nahum, L. H.: Changes of the Carbohydrate Metabolism of the Heart Following Coronary Occlusion. *Am. J. Physiol.* 109: 403, 1934.

Observations were made on 34 dogs during experimental coronary occlusion. The infarcted area lost appreciable quantities of its glycogen which appeared in part as increased amounts of soluble carbohydrates and lactic acid. In most cases before occlusion, the heart removed lactic acid from the blood stream. After

the coronary artery was ligated the heart usually added lactic acid to the blood stream. The increased lactic acid production by the heart was probably due to a diminution of the O_2 supplied to the cardiac tissues. Glucose was absorbed from the blood both before and after the coronary occlusion. It is suggested that the accumulation of metabolites in the infarcted areas may be related to the subjective pain experienced during coronary occlusion.

Riseman, Joseph E. F., and Stern, Beatrice: A Standardized Exercise Tolerance Test for Patients With Angina Pectoris on Exertion. *Am. J. M. Sc.* 188: 646; 1934.

A simple and safe standardized exercise tolerance test is described for use in patients with angina pectoris. The results in a group of 57 consecutive patients with the clinical diagnosis of angina pectoris are presented. Exercise performed under the standardized conditions of the test induced attacks in 34 patients. These attacks were precisely like those experienced in daily life. When the standardized test was repeated, even months later, the same amount of exercise again precipitated an attack in the same individual.

Nineteen patients did not develop an attack under the standardized conditions. The diagnosis of angina pectoris eventually proved to be exceedingly doubtful in all but one of these patients.

Objective evidence is presented illustrating the influence of various environmental factors on the amount of exercise necessary to precipitate attacks of angina pectoris in patients with this condition.

The test affords a means of investigating angina pectoris and is of distinct value as an aid in diagnosing doubtful cases and in evaluating both the condition of the patient and the results of therapy.

Flaxman, Nathan: Heart Disease in the Middle West. *Am. J. M. Sc.* 188: 639, 1934.

The incidence of organic heart disease in the Cook County Hospital, Chicago, for the period from January 1, 1932, to June 30, 1933, was 1.7 per cent of the total hospital admissions and 7.2 per cent of the medical admissions. Of the 1,646 patients, 38 per cent died in the hospital during the stated period. This was 6.7 per cent of the hospital deaths and 14.4 per cent of the medical deaths.

In this study the common age for heart disease was the forty to sixty year period. It occurred most frequently in the sixth decade in the white patients and in the fifth decade in the colored patients. Hypertension was the most common cause of organic heart disease regardless of race or sex. Arteriosclerotic and rheumatic heart disease were more common in the white patients. Syphilitic and hypertensive heart disease were more common in the colored patients. Arteriosclerotic heart disease was five times more common in the white patients. Pulmonary emphysema as a cause of myocardial insufficiency was practically confined to white males.

The author comments that statistics on the incidence and etiology of heart disease must be classified on a better basis, the most representative statistics being based on large general hospital admissions. This comment is open to serious question, since an extremely large group of cardiac patients never find their way into hospitals, and such a group would be entirely exclusive from any statistical analysis.

Ruddock, John C.: Dilatation of the Left Auricle to the Right. *Radiology* 23: 397, 1934.

The author concludes from examination of cardiac roentgenograms, together with histories and postmortem examination of the hearts, that dilatation of the right side of the heart as shown and demonstrated by roentgenographic examination in compensated cases of mitral stenosis is due to enlargement of the left auricle. He believes that as the auricle enlarges and dilates, there is an encroachment posteriorly to the right side so that the left auricle enters into the formation of the right cardiac silhouette. Enlargement of the right side of the heart in decompensated cases as shown by roentgenographic examination is due to dilatation of the right auricle.

In roentgenograms of cases of mitral stenosis, the cardiohepatic angle is either acute or obtuse and is in direct proportion to the degree of decompensation. In cases in which compensation is complete, the dilatation of the left auricle causes an acute angle which will be shown by roentgenograms as the cardiohepatic angle. In cases in which there is a decompensation and a resulting dilatation of the right auricle, the angle is either right or obtuse.

Description of the roentgenograms should call attention to the cardiohepatic angle, and the presence of compensation or decompensation must be known before a correct interpretation of the heart contour can be made.

Hansen, Olga S., and Maly, Henry W.: The Heart After Phrenic Nerve Interruption. *Am. Rev. Tuberc.* 30: 527, 1934.

In an effort to evaluate the effects of unilateral diaphragmatic paralysis by phrenic nerve interruption and the associated intrathoracic changes upon the heart, 100 successive cases have had physical, electrocardiographic and x-ray observations before and after this operation at Glen Lake Sanatorium for tuberculosis. No other type of collapse therapy had been employed. Those with pleural effusion were discarded.

Electrocardiograms showed a change in the direction and amplitude of the QRS waves in sixty-five, slight in degree in all but ten (fifty-five), but enough to indicate a shift of the electrical axis toward the left in twenty-five (all but one after a left-sided operation), and toward the right in ten (all but one after a right-sided operation). P-waves changed only six times, and no evidence of auriculoventricular conduction delay appeared. T-wave changes appeared in twenty-three cases, ten times with an increased negativity in the significant leads, and thirteen with an increase of size or a decrease of negativity. No clinical or roentgenographic evidence of myocardial changes appeared, or of defective conduction through the ventricles.

The heart position was displaced from its preoperative position in sixty-nine cases. After right-sided operations there was a preponderance of shifting toward the left or healthy side (twenty-nine times out of thirty-seven). After left-sided operations the heart might be displaced to either side (fifteen toward the left and seventeen toward the right). Twice as many were displaced away from the collapsed side as toward it (forty-six and twenty-three). Comparing the direction of the deviation of the electrical axis with that of heart displacement revealed agreement in eleven and disagreement in twenty-three.

No evidence of heart damage or disturbance of function appeared.

Cohn, Alfred E., and Steele, J. Murray: Unexplained Fever in Heart Failure. *J. Clin. Investigation* 13: 853, 1934.

Observations of the behavior of certain cardiac patients with fever have brought into question the wisdom of assuming in instances of unexplained fever

the presence of an infectious process. For this reason, the records of 368 cardiac patients have been studied. Of 172 who presented symptoms or signs of heart failure, 153 exhibited on two or more occasions, elevation of the rectal temperature to at least 100° F. Usually the elevations were clearly associated with conditions generally recognized as accompanied by fever, but in 49 cases the occurrence of fever was without satisfactory explanation. In certain ones its development suggested an origin, at least in part, dependent upon heart failure itself.

It is pointed out that fever may occur during heart failure in the absence of evidence of infection or of the noninfectious conditions which have been enumerated and which are likewise associated with the development of fever. Results of bacteriological studies of material obtained by puncture of the lungs during life and from the lungs at autopsy in patients with heart failure accompanied by fever are presented. In a number of cases, signs of heart failure appear or begin to increase just prior to the occurrence of fever. Fever and the signs of heart failure disappear simultaneously. These relations suggest that the occurrence of fever in these instances is dependent upon mechanisms involved in heart failure itself.

Steele, J. Murray: Fever in Heart Failure. Relations Between the Temperatures of the Interior and the Surface of the Body. J. Clin. Investigation 13: 869, 1934.

Daily fluctuation of surface and rectal temperatures has been studied in normal individuals, in individuals during and after recovery from heart failure, and in a few individuals suffering from infectious diseases. The patients with heart failure were selected for study because they exhibited fever and because evidence of infection was sought but was not found. A fairly regular normal diurnal variation in the temperature of the extremities opposite in direction to that of the rectal temperature is described. The behavior of the temperature of the surface of the body, especially of the extremities, in the cases of heart failure which exhibit fever of unexplained source is different from that observed in patients with fever associated with infectious diseases. The temperature of the surface in cardiac patients is lower than that of normal individuals, while that of patients with infectious fever is as high as or higher than normal. The difference in behavior leads to the conclusion that elevation of rectal temperature in cases of heart failure need not be of infectious origin but may depend upon a variety of processes incident to heart failure itself.

Steele, J. Murray, and Kirk, Esben: The Significance of the Vessels of the Skin in Essential Hypertension. J. Clin. Investigation 13: 895, 1934.

The temperature of the skin of individuals suffering from arterial hypertension does not differ significantly from that of normal individuals. Diurnal variations in surface temperature regularly occur in individuals with arterial hypertension without significant change in arterial pressure. Elevation of arterial pressure in hypertensive individuals does not depend on, though it may be accompanied by, constriction of the arterioles of the skin.

Page, Irvine H.: The Effect of Renal Efficiency of Lowering Arterial Blood Pressure in Cases of Essential Hypertension and Nephritis. J. Clin. Investigation 13: 909, 1934.

The efficiency of the kidneys, as measured by the urea clearance test, is not altered by a marked fall in arterial blood pressure occurring spontaneously or

induced by sodium thiocyanate administered by mouth, or colloidal sulphur administered intramuscularly, in patients suffering from essential hypertension. Sodium thiocyanate or colloidal sulphur in the dosage employed and over short periods of time does not appear to have a detrimental action on the kidneys of patients suffering from essential hypertension.

Fall in arterial blood pressure occurring spontaneously or as the result of renal denervation in patients suffering from chronic Bright's disease also caused no change in renal efficiency. The abnormal elevation of blood pressure in these cases does not appear to assist in maintenance of renal efficiency. This evidence does not support the compensatory theory of the cause of hypertension in patients suffering from nephritis or essential hypertension.

Kountz, W. B., Pearson, E. F., and Koenig, K. F.: Observations on the Effect of Vagus and Sympathetic Stimulation of the Coronary Flow of the Revived Human Heart. *J. Clin. Investigation* 13: 1065, 1934.

The effect of vagus and sympathetic nerve stimulation on coronary flow was studied in the revived human hearts and in the same hearts arrested by alkaline and acid perfusate. In the normal beating human heart, vagus stimulation slowed the heart rate and increased the coronary flow. Sympathetic nerve stimulation increased the heart rate and slowed the coronary flow.

In hearts in which there was dissociation of auricular and ventricular contraction and in which the rate was not influenced by the nerves, vagus stimulation slowed the coronary flow, while sympathetic stimulation increased it.

In hearts arrested with increased tone, vagus stimulation increased the coronary flow while sympathetic stimulation in two cases decreased it. In hearts arrested in decreased tone by acid perfusate, vagus stimulation had no effect, while sympathetic stimulation increased the flow.

The action of the nerves in these hearts was compared to that of drugs. It was found that drugs which in the beating heart increased muscle action and decreased coronary flow closely simulated the action of the sympathetic; while drugs which dilated the beating heart and increased coronary flow simulated vagus nerve stimulation. No such similarity was noted between nerve action and drugs which act primarily as vasoconstrictors or vasodilators of the coronary vessels themselves.

The results of this group of experiments suggest that in man the cardiac nerves exert their most important action on coronary flow through changes in the state of the heart muscle.

Donal, John S.; Gamble, Clarence J.; and Shaw, Robert: The Cardiac Output in Man. *Am. J. Physiol.* 109: 666, 1934.

The katharometer has been adapted to the measurements of ethyl iodide in air required by the procedure of Starr and Gamble for determining the cardiac output in man. The average error of a determination of the relative concentration of ethyl iodide in the range in question is ± 0.04 mg. per liter or ± 0.0006 per cent by volume.

The instrument permits a marked saving in the operator's time required. A duplicate determination of cardiac output including the analyses and calculation of results may be made in seventy minutes. Cardiac outputs in the lying, sitting, standing, and inverted positions have been compared in fasting subjects at rest. The average value in the sitting position was 87 per cent and in the standing position 82 per cent of that when lying. The corresponding values for the output per beat were 76 and 60 per cent. In all the cases the arteriovenous oxygen

difference was greater in the erect than in the horizontal position. In the vertical position with the head down, the cardiac output per minute and per beat was less and the arteriovenous oxygen difference greater than when the subject was horizontal.

Comparisons are given of other circulatory and respiratory values in the various positions.

Proger, S. H., and Dexter, L.: *The Continuous Measurement of the Velocity of Venous Blood Flow in the Arm During Exercise and Change of Posture.* *Am. J. Physiol.* 109: 688, 1934.

The method recently described by Gibbs has been found useful and practicable as a means of measuring continuously the relative velocity of blood flow and in certain instances qualitative changes in volume flow. In cases in which it is desired to record changes in velocity in a vessel which is visible, a solid needle in which hot and cold thermo-junctions have been incorporated has certain advantages over an open needle into which the thin wires containing the junctions are threaded after venipuncture.

The velocity of blood flow in the superficial and deep veins of the arm behave antagonistically with exercise of that arm, the flow in the deeper veins becoming more rapid and in the superficial veins slower than at rest. With moderately severe exercise involving chiefly the lower extremities (pedalling on a stationary bicycle), there is no change in the velocity of blood flow in the veins of the upper extremities. In the superficial and deep veins of the upper extremities, the velocity of blood flow is slower with the arm held in the erect position and more rapid with the arm hanging down, than when the arm is in the horizontal position.

Padilla, T., and Cossio, P.: *Prognosis in Myocardial Infarcts.* *Rev. Argentina de Card.* 1: 181, 1934.

Mortality in this series of cases has been 38 per cent, which is somewhat lower than that of other observers. A great majority of deaths occurred during the first month following the attack. Nineteen per cent of the patients died within forty-eight hours, and 14 per cent died between that period and the end of the month. Within the first twenty-four hours, death occurred suddenly and probably was due to ventricular fibrillation; rupture of the heart was exceptional.

After fifteen days from the beginning of the attack and within the first year, death was due to cardiac insufficiency; embolism was exceptional. After one year, death may be caused by a new cardiac infarct or by any other arterial accident.

After one month from the beginning of the attack, 27 per cent of the cases were clinically cured and 35 per cent were so after a six months' period. Six months after the attack, slight symptoms persisted in 17 per cent of the cases. In 9 per cent, congestive heart failure could be observed, and 5 per cent suffered from angina pectoris. Death occurred in 60 per cent of the patients suffering from a second attack of infarction.

Sex and age made no difference so far as prognosis is concerned. The absence of pain has severe prognostic significance. Intense pain was present in a large proportion among the patients who survived, 72 per cent, than among those who died. The absence of circulatory collapse has a favorable prognostic significance. The early appearance of cardiac failure, the appearance of an indefinite discomfort sensation with or without precordial oppression and the absence of electrocardiographic disturbance have a severe prognostic significance. Electrocardiograms of the apex type (T_1) or the base type (T_2) have no particular prog-

nostic significance. If both types occur at the same time, prognosis becomes severe. Disturbances of rhythm, other than isolated extrasystoles, have an unfavorable prognostic significance.

Battro, Antonio, and Del Rio, Julio G.: Lead IV in Electrocardiography. *Rev. Argentina de Card.* 1: 192, 1934.

Systematic use of Lead IV has led to the following conclusions:

Lead IV should be recorded in all anginal syndromes: in four out of twenty patients with angina, there was definite electrocardiographic evidence of myocardial infarction in Lead IV, while the conventional leads were practically normal. Lead IV has also proved of value in determining complexes which are not far from normal in the conventional leads but which are true extrasystoles in Lead IV. Lead IV, however, does not allow a clear distinction between right and left ventricular extrasystoles. Right bundle-branch block showed a concordant positivity of the main initial deflections in Lead IV and Lead I. Conversely, left bundle-branch block showed a concordant negativity of the main initial deflections in the same leads.

Rivolta, L. A.: Radiograms of the Heart in Systole and Diastole. *Rev. Argentina de Card.* 1: 216; 1934.

A device is described to obtain radiographs of the heart during either systole or diastole. The electrical disturbance caused by the heart sounds are amplified in a microphone adapted to the precordial region, starts the x-ray machine. Mechanisms are provided which allow an accurate adjustment so as to take the radiograph at any desired moment after the beginning of cardiac activity during either systole or diastole. When the heart sounds are modified in their number or quality, the central arterial pulse can be substituted to start the x-ray machine.

A characteristic feature of this method consists in the actual mechanism of starting the x-rays which is very closely associated with cardiac activity (heart sounds or central pulse) thus avoiding the several causes of error that are encountered in following other procedures so far described.

Paul, John R.; Harrison, Elizabeth R.; Salinger, R.; and DeForest, G. K.: The Social Incidence of Rheumatic Heart Disease. *Am. J. M. Sc.* 188: 301, 1934.

In an attempt to determine the influence which poverty and urban environments may play as predisposing factors in rheumatic fever, the incidence of rheumatic heart disease has been determined in groups of children between the ages of five and eighteen years, attending urban and suburban schools in and about the city of New Haven.

Data from the routine examinations of 5,758 public school children performed by school physicians suggested that systolic murmurs, presumably of rheumatic origin, were roughly 1.5 times as prevalent among children from the poorer districts than in those from the better districts of the city.

From the authors' examination of 758 urban children, the incidence of rheumatic heart disease in a single large public school in one of the poorest districts of the city was found to be 48.1 per 1,000. This proved to be 1.5 times as high as that found in a public school in one of the better districts of the city, but 8 times as high as that found among a smaller group of pupils from urban private schools who came from the best districts of the city.

The average incidence of rheumatic heart disease among pupils attending two urban public schools was about twice that recorded among pupils of a similar age group who attended suburban and rural public schools.

Ernstene, A. Carlton; and Mulvey, Bert E.: A Study of Auricular Fibrillation Following Operations for Goiter. *Am. J. M. Sc.* 188: 382, 1934.

Sixteen of 213 patients with hyperthyroidism had auricular fibrillation during the preoperative period; while postoperative auricular fibrillation developed in 31 of the 197 who had normal rhythm before operation. The arrhythmia was present before operation in 2 of the 192 individuals who had adenomatous goiter without hyperthyroidism and developed after operation in 4 other patients in this group.

The age of the patient, type of goiter, and duration of hyperthyroidism appear to be the most important factors predisposing to the development of postoperative auricular fibrillation. The degree of elevation of the basal metabolic rate is of little significance. The immediate increase in the rate of metabolism following operation probably is the essential factor responsible for the initiation of the arrhythmia.

Postoperative auricular fibrillation is more common in thyrotoxic patients with adenomatous goiter than in those with hyperplastic goiter. This difference cannot be explained entirely by differences in the ages of individuals belonging to the two groups. The long duration of thyroid enlargement in the majority of patients with adenomatous goiter may favor the gradual development of myocardial damage, possibly as the result of repeated or prolonged periods of low grade, unrecognized hyperthyroidism.

Postoperative auricular fibrillation generally begins during the first sixty hours after operation. It rarely causes circulatory embarrassment, and normal rhythm usually is reestablished spontaneously within forty-eight hours.

Korey, Herman, and Katz, Louis N.: The Electrocardiographic Changes Produced by Injuries of Various Parts of the Ventricle. *Am. J. M. Sc.* 188: 387, 1934.

An analysis was made of the changes produced in the electrocardiogram during the first four hours following injection of 95 per cent alcohol into the dog's ventricular myocardium with the production of sharply demarcated areas of injury. Within a few minutes following injection of alcohol into the myocardium, monophasic ventricular complexes occurred several times. Deep inverted or tall upright peaked T-waves having rounded shoulders and symmetrical limbs—negative and positive coronary T-waves—were frequently found later. In addition to the T_1 and T_2 types of curves, two other types of change which we have called the T_p and T_n types occurred frequently. In the T_p type, positive coronary T-waves occurred in all three leads preceded by negative S-T deviations. In the T_n type negative coronary T-waves appear in all three leads preceded by positive S-T deviations.

On subdividing the ventricular myocardium into ten regions, it was found that the location of the myocardial lesion did not determine the magnitude of the electrocardiographic change, nor did it give rise to a characteristic Q-T type of change for any locality. It is concluded that using the standard three leads, the electrocardiogram cannot be used to differentiate between injury to the anterior and the posterior wall of the ventricle; between injury to the right and the left ventricle, and between injury to the apical and the basal portion of the ventricle. No constant correlation could be made between the size of the injured area and the magnitude of electrocardiographic change in the standard three leads. The electrocardiographic changes apparently do not depend upon the location of the injured area in relation to the endocardium or epicardium.

Book Reviews

VERHANDLUNGEN DER DEUTSCHEN GESELLSCHAFT FÜR KREISLAUFFORSCHUNG. VII TAGUNG. Edited by Professor Doctor Eb. Koch, Bad Nauheim. Theodor Steinkopff, Dresden and Leipzig, 1934, 326 pages.

The Transactions of the seventh (1934) annual session of the German Society for the Study of the Circulation maintain fully the high standards of those of the earlier meetings. The topics given special consideration are those of thrombosis and embolism. Most of the volume of more than three hundred pages is devoted to the various aspects, experimental, pathological, clinical, of these subjects; and the character of the presentations is indicated by the fact that among the many contributors are to be found such distinguished students of these conditions as Aschoff, Mosawitz and Dietrich.

L. A. C.

PRACTICAL TALKS ON HEART DISEASE. By George L. Carlisle, Associate Professor of Clinical Medicine, Baylor University, Dallas, Texas. Springfield, 1934, Charles C. Thomas, 153 pages.

This small book was written expressly for the general practitioner, and the author's purpose is manifest throughout. There are many features that should receive warm commendation; among these may be mentioned brevity, clarity, and refreshing sanity with respect to most of the subjects treated. The comments upon history taking, physical examination, and the interpretation of abnormal signs are pointed, emphatic, and thoroughly sound. His brief discussions of the four common etiological types of heart disease indicate his agreement with modern views, and are probably as satisfactory for the general practitioner as any very brief consideration of the subject could be.

There are, however, certain deficiencies that greatly lessen the value of the book, and it is unfortunate that the sections dealing with treatment are particularly inadequate or actually misleading. For example, the treatment of paroxysmal tachycardia and of auricular flutter is dismissed with a few words, and the most effective forms of treatment are not mentioned. The treatment of auricular fibrillation is discussed in a single sentence, which states that the only treatment is that of decompensation "because in treating decompensation, you are almost always treating auricular fibrillation." It is strange that a writer so obviously familiar with recent work in the field of heart disease should advise the regulation of digitalis dosage entirely on the basis of the heart's rate, and should make no distinction between cases of regular rhythm and of auricular fibrillation. His discussion of the treatment of angina and of coronary thrombosis is extremely misleading, and it is clear that he does not distinguish properly between the two conditions; for example, he treats anginal attacks with morphine, insists upon two months of complete bed rest, and says practically nothing about the future regulation of the patient's life, or of the use of nitrites. He has a number of excellent things to say about cardiac neuroses, but with respect to this subject also his advice about treatment seems quite superficial and unsatisfactory. It is deplorable that a book which displays

so much wisdom should summarize this important matter with the words: "The treatment of cardiac neurosis consists in out-talking the patient over a long period of time."

While these are serious defects, it would be unfair to leave the impression that the book fails entirely in its purpose. There is so much of value and importance that it is to be hoped the next edition will correct the relatively few omissions and errors.

H. M. M.

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Original Communications

LOCALIZATION OF CARDIAC INFARCTS ACCORDING TO COMPONENT VENTRICULAR MUSCLES*†

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ON REVIEWING the literature of the past fifteen years one is impressed by the number of attempts to correlate the electrocardiographic findings with the anatomical lesions found in cases of coronary thrombosis. We are probably not minimizing the truth when we say that success has not been great. All these attempts at localization have been made either in terms of topography of the heart, e.g., right or left ventricle, anterior or posterior surface, base or apex, etc., or in terms of the larger branches of the coronary arteries, as the descending or circumflex branch of the left coronary, etc.

We have approached the problem from a different angle, using the individual ventricular muscles as a basis. There have been many attempts to divide the heart muscle into its component bundles, the most noteworthy being those by MacCallum,¹ Mall,² and Tandler.³ Robb⁴ has recently repeated this work and is adding to it a study of the coronary supply to each muscle band. She noted that many of the smaller vessels supplied only one or predominantly one of these muscle bundles, in this respect resembling the end arteries to skeletal muscle. In subsequent experiments advantage was taken of this one-muscle distribution to produce a localized ischemia by ligating these end arteries in 21 dogs. The immediate effects upon the electrocardiogram and on the blood pressure

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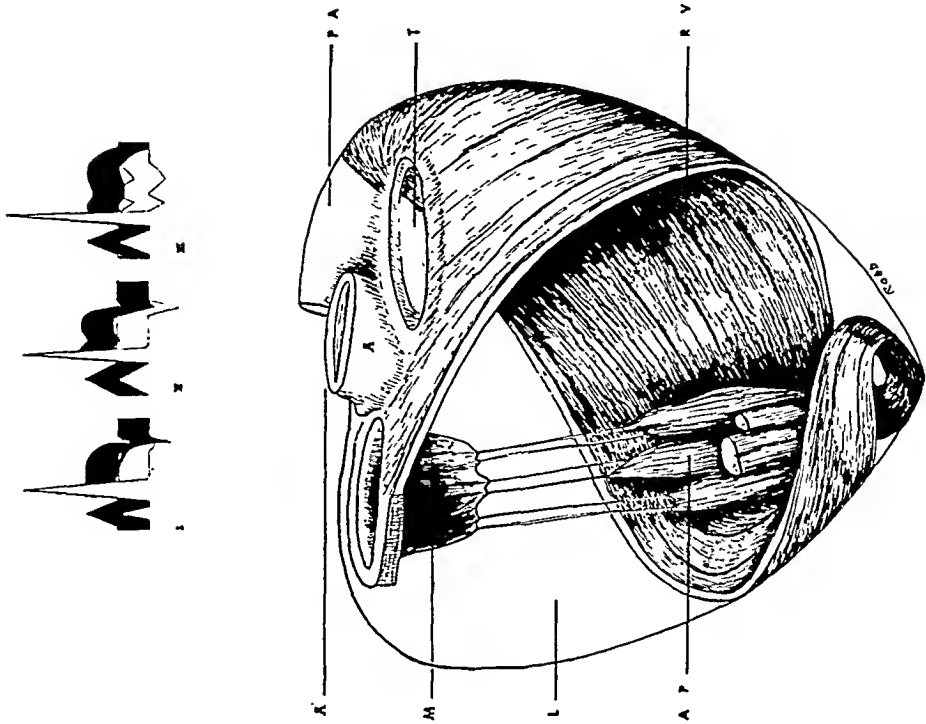


Fig. 2.

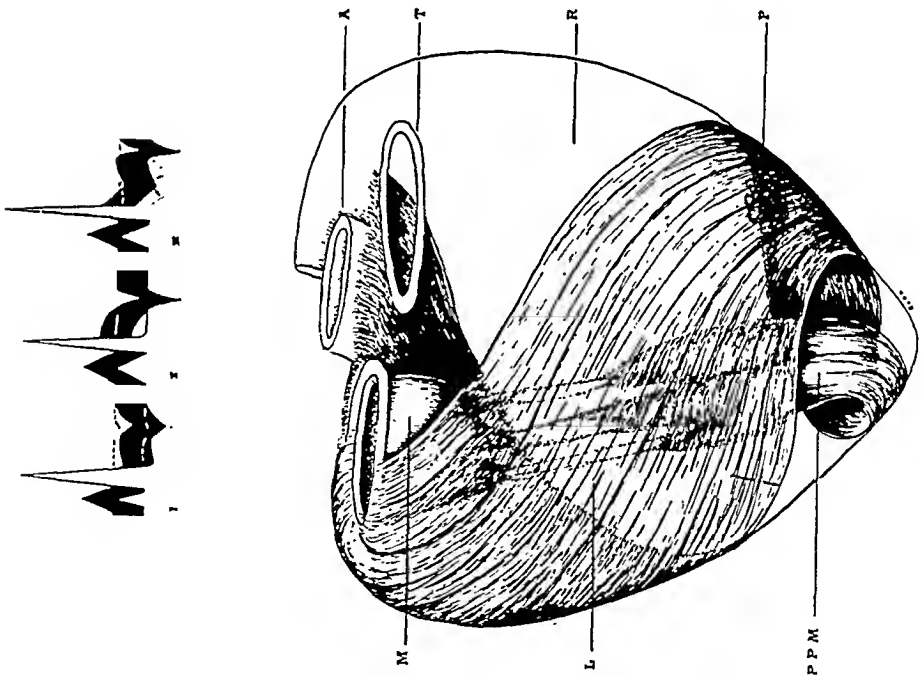


Fig. 1.

Fig. 1.—Superficial bulbospiral muscle, posterior view. Origin from portions of the left A-V ring. Insertion, mainly through the posterior papillary muscle and the posterior leaflet of the mitral valve to the left A-V ring. Certain of the branches of the anterior and posterior descending coronary arteries are "end arteries" to the internal portion of this muscle. The characteristic electrocardiogram for injury to this muscle shows depression of R-T in Lead I and elevation of R-T in Leads II and III.*

Fig. 2.—Superficial sinospiral muscle, posterior view. Origin mainly from the right A-V ring. Insertion, mainly through the anterior papillary and anterior leaflet of the mitral valve to the left A-V ring. Branches of the anterior descending coronary artery are "end arteries" to the internal portion of this muscle. The characteristic electrocardiogram for injury to this muscle shows slight elevation of R-T. In all leads.

were noted. Four of the six ventricular muscles are available for such a study, e.g., the superficial sinospiral, superficial bulbospiral, deep sinospiral, deep bulbospiral.

As a complete control for each ligation, after the heart had been removed, the ligated vessel was injected with a dye, just distal to the ligation. The heart was then dissected so that it could be established that in a particular case the blood vessel in question did supply only the one muscle and that the resulting electrocardiogram was due to injury of that muscle alone.

Four types of muscle injury have been studied: (1) ischemia, (2) compression, (3) cutting, (4) injury to the internal attachment of the muscle (probably injury to the Purkinje material) by an instrument inserted through the auricular appendage and passed down into the ventricle. Regardless of the type of injury the electrocardiographic changes are consistent for each muscle. A few attempts were made to use freezing as a method of injury, but were discarded since it was not possible to localize the temperature change to one muscle.

Blood pressure was recorded through a carotid cannula and a mercury manometer. Injury to the superficial muscles caused little fall in blood pressure, usually less than 5 mm. of mercury. Injury to either of the deep muscles caused a fall in blood pressure, equal to 20 per cent to 50 per cent of the original value. If several vessels were ligated in rapid succession, death was immediate.

The details of the findings are presented in Figs. 1-4 and their legends. Because of limited facilities it was not possible to carry on chronic experiments, hence it must be emphasized that the results given are for acute experiments lasting up to ten hours.

DISCUSSION

Fortunately some experiments by other investigators are so well reported and illustrated (especially those of Fred Smith and his co-workers⁵) that we do have some idea of the after effects of lesions of individual muscles. It is interesting to note that both Smith,⁵ and Barnes and Mann⁶ obtained electrocardiograms similar to ours when the only manipulation consisted in opening the pericardium. Both investigators state, however, that at autopsy there was in each case a definite acute myocarditis involving the superficial muscle fibers, thus illustrating another method of muscle injury which causes the same characteristic changes in the electrocardiogram.

^{*}In each illustration, I, II, and III indicate the corresponding leads. The dotted lines indicate the normal control.

A, aorta; A P, anterior papillary muscle; L, left ventricle; M, mitral valve; O, origin of deep sinospiral muscle; P, fibers to the right anterior papillary; P A, pulmonary artery; P P M, posterior papillary muscle; R V, right ventricle; S, scroll muscle; T, tricuspid valve. The electrocardiograms are redrawn to scale; the muscle sketches are diagrammatic.

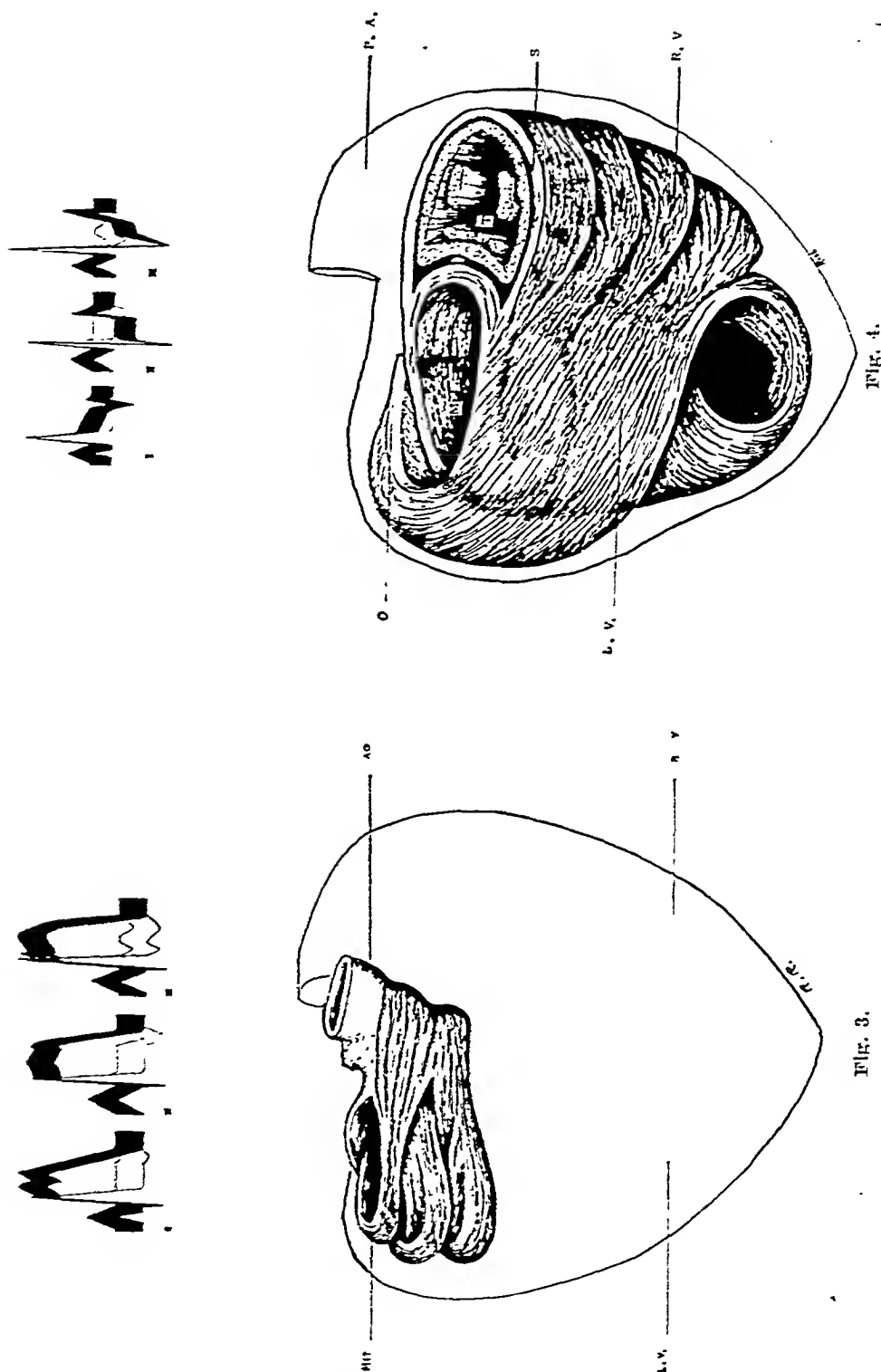


Fig. 3.—Deep bulbospiral muscle, posterior view. A constrictor muscle surrounding the base of the left ventricle. Blood supply from branches of the left circumflex. The characteristic electrocardiogram for injury to this muscle shows marked elevation of R-T in all leads.

Fig. 4.—Deep sinospiral muscle, posterior view. Origin, nearly the whole circumference of both A-V rings. Insertion, into all papillary muscles of the right ventricle and to the anterior wall of the left ventricle by fusion with the superficial sinospiral. Blood supply from a branch of the anterior descending coronary and from lateral branches of the right coronary. The characteristic electrocardiogram from injury to either the right or left portion of the muscle shows an elevation of R-T in Lead I and a depression of R-T in Leads II and III.

We have been fortunate in having some human material to study correlating specific muscle lesions with their electrocardiographic manifestations, and at the present time we are of the opinion that the result of experimental work on dogs will eventually be confirmed in man. Because of the fact that the human heart, in order to be of any value to us, must have a lesion in one muscle only, must have an early electrocardiogram, and must then come to autopsy, and at the autopsy the heart must be given to us intact so that we can inject it and study it by very careful dissection, our material is necessarily very limited. An ordinary post-mortem heart examination not only is of no value for muscle localization, but very definitely prevents a proper study of the case. A plea is therefore made that wherever material is available it be studied with special reference to lesions in the various muscles, for only in this manner can it be determined whether our experimental findings are applicable to man.

It would appear that lesions of the two superficial muscles demand less protracted treatment and offer a far better prognosis than do those of the deep muscles.

These experiments on dogs indicate that localization of coronary lesions is possible by the electrocardiograph if one localizes according to the muscle bands. The type of muscle injury is unimportant. Data have been presented previously (Robb⁷) to prove that if any lesion involves all the cross-section of the muscle, a further lesion in another area (still having an adequate blood supply) may cause no further change in the electrocardiogram. Mention has already been made of the fact that the electrocardiogram for elimination of the deep sinospiral is constant regardless of whether the left or right portion of the muscle is involved. These results cannot be explained according to the current description of the physiology of conduction in the ventricle.

CONCLUSIONS

1. Certain coronary branches are "end arteries" to the individual ventricular muscle bands.
2. If such end arteries are ligated, the resulting infarcts affect the electrocardiogram consistently.
3. Elimination of either or both of the superficial muscles alters the blood pressure little or not at all.
4. Elimination of either of the deep muscles causes a marked fall in blood pressure, and if the lesion be large, death is immediate.
5. These results cannot be explained according to present-day conceptions of the physiology of conduction.

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NONPENETRATING WOUNDS OF THE HEART

A CLINICAL AND EXPERIMENTAL STUDY*

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PROBABLY the most common type of trauma to the heart is that produced by stab or bullet wounds. However, there is another type of cardiac trauma produced by contusive or compressive forces, and it is this type of nonpenetrating cardiac wound that we shall discuss in this paper.

One is accustomed to look upon the heart as an organ which almost always escapes any of the ordinary injuries to which the rest of the body is subjected. The thoracic cage affords what is usually considered to be practically a perfect protection to the heart. No such immunity to injury from contusive or compressive forces is extended to the liver, spleen, kidneys, brain, and other organs of the body. It is remarkable that this belief has developed, because the heart, lying against the sternum, is vulnerable to any sudden impact over the sternum and, buttressed against the bodies of the thoracic vertebrae posteriorly, is vulnerable to compression forces applied to the chest. There can be little doubt that the heart is the recipient of many injuries. Most of these probably produce no functional disturbances and are not recognized. Some of them do produce functional disturbances, and usually these are not recognized.

We have attempted to review all cases of nonpenetrating cardiac wounds that have been reported.† The entire literature on the subject, however, was not available to us, so that our study, while extensive, is not complete. We have excluded from our analysis those cases in which the injury produced a rupture of a valve without showing other manifestations of cardiac injury. This group was excluded because a rupture of the valve seems to offer no possibility for operative repair.‡ We have excluded also those cases of rupture of the

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‡We do not want to imply that the operative repair of a cardiac valve is entirely beyond the realm of possibility. We should remember that operative surgery, as we know it today, is very young. Although surgery has an ancient ancestry, nevertheless our modern methods of operating are not old. We do not want to underestimate the operative methods that were established centuries ago, but is it not true that surgery just learned to stand up and walk, so to speak, in the 80's and 90's of the last century? And is it not true that the development of some of the more difficult technical procedures, such as some of the intracranial and intrathoracic operations, had to wait twenty-five years until Lister's child learned its alphabet? It is not inconceivable that technical methods may develop so that operations can be done, not only on the surface of the heart as they are today, but also in the cavity of the heart.

heart that followed myocardial infarction due to coronary occlusion. This group was omitted because the rupture in cases of myocardial infarction is not traumatic in origin. The group of cases designated as cardiac strain also was excluded. This group may be related to the general one of nonpenetrating trauma so far as the possible rôle of increased intracardiac pressure is concerned. The symptoms may be similar, but evidence of trauma is not demonstrable at autopsy in cases of heart strain.

On the basis of our analysis we can give in outline form the various ways by which nonpenetrating wounds of the heart were produced.

- I. A direct blow over the precordium producing fracture of sternum or ribs, the broken ends of which were driven into the heart.
 - a. A cavity of the heart may be penetrated (Heger-Houbotte).
 - b. The myocardium may be penetrated, rupture taking place days, weeks or months later (Groom), or the wound may heal with recovery or an aneurysm of the heart may develop later (Joachim and Mays).
- II. Contusion or compression of the heart between the sternum anteriorly and the vertebrae posteriorly. This space is occupied almost entirely by the heart, and any decrease in it directly affects the heart.
 - a. The heart may be ruptured. The ribs and sternum may be fractured (Kennedy, Ferris), or they may not be fractured (McOscar and Voelker, Hutchinson, Godlee, Bilderbeck).
 - b. The heart may be bruised but not ruptured, and it may or may not show functional derangements later.
- III. The application of indirect forces, such as by the sudden compression of the legs and abdomen (Kellert, Stephens, Copeland).
- IV. Laceration of the thoracic viscera, such as may be sustained in a fall from a high building (Robertson, Heger-Houbotte, Schütt).
- V. Concussion of the heart. Although this term has been used by several writers, we are unable to determine from the literature whether the heart can be disturbed by concussive forces. The distinctive feature of a concussive injury is that it is usually produced by a force of rapid motion without bringing about demonstrable pathological changes. One can assume that functional alterations in the conduction mechanism of the heart may take place without showing organic changes. It is possible that stimuli resulting from trauma and transmitted through the vagus nerves can stop the heart. In the case reported by Lee and Downs the heart stopped when traction was exerted upon the stomach. In the case reported by Glover the heart stopped when a gland was dissected from the root of the

mesentery in the duodenojejunal angle. These probably were instances of vagus stimulation.

The cases that we analyzed can be classified into three groups: (1) the group of patients that survived the trauma; (2) the group that died of myocardial failure; (3) the group that died of rupture of the heart.

GROUP I. PATIENTS WHO SURVIVED THE TRAUMA

Inasmuch as the patients in this group survived the trauma, the diagnosis of cardiac involvement was made on clinical manifestations. The group includes twelve cases.

CASE 1.—Hochhaus, quoted by Loison. Case briefly referred to by Loison was a man forty-three years old who was struck by a plank and sustained fractures of several ribs. Circulatory decompensation developed after the accident, but the patient recovered.

CASE 2.—Lückinger, 1893. Patient, a male twenty-five years old, fell from a load of straw and struck the left side of the chest. No evidence of fractured ribs or sternum. Five days after the fall patient developed dyspnea and palpitation of the heart. A pericardial friction rub and a systolic and a diastolic murmur could be heard. On the following day these signs and symptoms disappeared, and the patient recovered.

CASE 3.—Moullin, C. W. Mansell, 1897. Patient, a male twenty-three years old, was injured while playing football. The injury was inflicted by an opponent's elbow striking against the third left intercostal space. He continued with the game for twenty minutes after the accident. Then he collapsed. Twenty-five days after the accident the patient was critically ill. The area of cardiopericardial dullness had increased, the cardiac sounds were distant, cyanosis was marked. An incision was made in the fifth interspace on the left side and the pericardium incised. Six pints of thin, dark fluid were removed from the pericardial cavity. Patient recovered and was in good health.

So far as we have been able to determine, this was the only case of nonpenetrating injury in which the operation of pericardiostomy was carried out. In this respect it is unique. Whether the heart sustained a bruise was not determined by the operation. It would seem that the exposure was too limited to afford adequate examination of the heart to determine whether or not there was a contusion of the myocardium. Experimentally a hemorrhagic effusion not uncommonly develops after the myocardium has been bruised.

CASE 4.—Rosenson, 1924. Patient was a boy ten years old who three years before had received a hard punch over the precordium. Immediately after the trauma the child became weak and experienced a fluttering sensation in the region of the heart. He was unable to walk. Two days later he attempted to walk, fell, and became unconscious. Examination showed pallor of the skin, slight dyspnea, and a heart of normal size. The electrocardiogram showed partial (?) heart-block, a rapid ventricular rate, P-R interval 0.28 second, P- and T-waves fell together. The patient was kept in bed for two weeks, and at that time the heart returned to normal rhythm. During a three-year period of observation the heart remained normal. The author asks the question whether the lesion in this case was a slight hemorrhage in or about the node of Tawara, and he makes the comment that there is no similar case reported in the literature.

CASE 5.—Levison, 1927. Patient was a male twenty years old who received a crushing injury to his chest, having been compressed between two trucks. There were no fractures. The patient immediately had severe pain over the precordium, marked dyspnea but no cyanosis. Auricular fibrillation with a pulse rate of 150 per minute developed. Dyspnea was increased by exertion. The electrocardiogram taken thirty-six hours after the accident showed normal mechanism, and abnormally large T-waves in all leads. The patient made a complete recovery. All signs and symptoms of a cardiac nature disappeared.

CASE 6.—Yates, 1916. Patient was a farmer, forty-six years old, who was thrown out of a wagon by a runaway team. The fourth and fifth ribs on the left were fractured. The chest wall was depressed over the axillary region on the left side. The patient complained of pain in the chest. He had marked dyspnea. A loud splashing sound was heard with each heartbeat, and it was believed that hemopericardium was present probably from a rib penetrating lung and pericardium. This sound persisted for ten days. The patient was critically ill for two weeks. He then recovered and was up and about three weeks after the accident.

CASE 7.—Kahn and Kahn, 1929. A woman thirty-two years old weighing only 82 pounds slipped and fell forward, striking the sternum against the corner of a table. Immediately after this accident she felt severe, sharp pain in the precordium. Tachycardia, dyspnea, and palpitation of the heart also developed. These symptoms were sufficiently severe to make the patient go to bed. Six months after the accident she still had marked precordial and sternal tenderness, dyspnea, palpitation of the heart on exertion, a murmur heard at the apex, and disability due to the sternal pain. The electrocardiogram was normal. The authors did not claim that this case necessarily was an example of a cardiac contusion.

CASE 8.—Kahn and Kahn, 1929. A man, fifty-five years old, was hit over the left lower ribs by a truck. He was unconscious for a short period of time; he had intense pain in the left lower abdomen, and an aching, numb sensation in the left hypochondriac region. That night the sharp, localized pain in the left lower ribs became worse, especially on deep breathing. He was dyspneic and had palpitation. Two days later pleurisy was diagnosed. One month after the accident the patient had a sudden severe localized gripping pain over the left lower ribs. Similar attacks of pain were accompanied by palpitation of the heart and dyspnea. Four months after the accident the patient was well except for tenderness to pressure over the cardiac apex. "Apparently the injury produced no permanent affection of the heart, although the symptoms and the attacks that the patient suffered from may be attributed to some direct trauma to the heart."

CASE 9.—Kahn and Kahn, 1929. This patient was a man forty-nine years old who tripped and fell heavily to the ground. Later in the day he felt some tightening in the chest and had a little difficulty in breathing. That evening he had dyspnea, which was worse the next day. "He remained in bed for a month after the diagnosis of acute pericarditis was made." A month after the accident he had dyspnea and a slow pulse of small volume. The heart sounds were somewhat muffled. The brachial arteries were somewhat tortuous. The electrocardiograms showed normal sinus rhythm, left ventricular preponderance, inversion of the T-wave in Lead I, and the P-wave isoelectric in Lead III. The patient "resumed lighter work for five months or more before he died rather suddenly [i.e., about ten months after the accident]. Whether or not the coexistence of acute coronary closure figured in its production must remain speculative."

CASE 10.—Kahn and Kahn, 1929. A man thirty-three years old was struck over the front of his chest by a plank of lumber which fell from a scaffold 18 feet above the ground as the patient was looking up. The patient fell backward, was momentarily dazed, got up but was so weak that he had to lean against the building. He had dyspnea, and as he walked he was weak and dizzy. He worked half of the following day. He spent the next two weeks in a hospital. Examination three months after the accident showed auricular fibrillation with a rate of 150 per minute. "There was an indication of left ventricular preponderance. Premature beats occurred singly or in groups, arising probably in the auricular wall in the region of the A-V node." The arterial pressure was 104 mm. Hg systolic and 78 mm. diastolic. Normal sinus rhythm was restored after the administration of quinidine sulphate. Six months after the accident recovery was complete. All symptoms had disappeared. The authors stated that "the pathological changes that may have taken place from the injury are necessarily speculative. The possibility of subepicardial ecchymosis in the auricular muscle is to be considered."

CASE 11.—Kahn and Kahn, 1929. A truckman sixty-three years old while lifting a heavy weight fell and struck his chest on the end of a wagon. He was unconscious for a few minutes after the accident and then resumed his work. For the next two days he was in bed; his condition became worse, and four months after the accident he was placed in a hospital. At that time he had auricular fibrillation. Myocardial failure resulted in death five months after the accident. The authors concluded that "the patient showed arteriosclerotic myocardial disease and auricular fibrillation. If the fibrillation had existed prior to the injury, the man would have had some distress or inability to do his work. In the absence of this we are compelled to attribute the onset of fibrillation to the direct trauma to his chest that he suffered in the fall."

CASE 12.—Tuohy and Boman, 1931. A man seventy years old while carrying a weight of 100 pounds on his shoulder tripped and fell down a stairway, striking his thorax a stunning blow. He was not unconscious. He suffered severe precordial pain. There were no fractures. An electrocardiogram taken five weeks after the accident showed complete heart-block. One taken after another interval of five weeks showed normal sinus rhythm but right bundle-branch block. This condition lasted for about ten days, when complete block returned. The authors present this query, "What was the relationship of his injury to this decisive interference in his conducting mechanism? The answer could be more dogmatically given could the interventricular septum be carefully examined. Two general hypotheses present themselves: This seventy-year-old man came by his conduction disturbance through the usual route of myocardial fibrosis with localization in the interventricular septum and affecting the bundle of His independent of his injury; or the injury induced traumatic sequences, the most likely of which is hemorrhage into the same area."

GROUP II. PATIENTS WHO DIED OF MYOCARDIAL FAILURE

This group includes those cases in which death occurred from myocardial failure. The diagnosis was made by necropsy examination. The group consists of 11 cases. The cases reported by Blancard (1688) and Akenside (1764)—both quoted by Fischer—were excluded from this group because it could not be determined whether trauma or infection was responsible for the changes in the heart.

CASE 1.—Watson, quoted from Fischer. We were unable to find this article. The case was referred to briefly as one in which the sternum was fractured, the pericardium torn, and the myocardium bruised.

CASE 2.—Casper, 1857, quoted from Fischer. A male, sixty-six years old, was knocked down by a falling sack of corn. One femur was fractured and the leg was amputated. Death occurred eight days later. The necropsy examination showed fractures of the third thoracic vertebra and several ribs. An extensive hemorrhagic area in the wall of the left ventricle was found, measuring about 2 inches in diameter.

CASE 3.—Markham, 1858. This patient was a man who was injured in a fall from an omnibus. Death resulted from hemorrhage in the brain. A bruise the size of a silver dollar was found in the interventricular septum.

CASE 4.—Werner, 1873. This patient was a child three years old who was ground under foot by a cow and died thirty-one hours after the accident. The pericardium was intact; there was no intrapericardial hemorrhage. Extravasation of blood was found under the epicardium. The myocardium was completely severed on the anterior wall of the left ventricle, leaving only the epicardium intact. Apparently the epicardium alone prevented the escape of blood from the cavity of the heart. The tear of the myocardium measured 14 mm. in length.

CASE 5.—Schuster, 1880. A healthy laborer, forty-three years old, received a blow on the chest by a harness bar and was thrown violently to the ground. He immediately recovered, but for a period of two weeks he had pain in his chest. While doing some heavy lifting he developed severe epigastric pain and a sensation of choking. The skin became pale, cold, and cyanotic. The pulse became weak and the patient died two hours after the exertion. The necropsy examination showed some extravasation of blood in the mediastinum and in the pericardial cavity. The left ventricular wall and the right auricular wall showed extravasation of blood. The right coronary artery and vein were surrounded by hemorrhage. According to the description these vessels were encroached upon by hemorrhage.

CASES 6 and 7.—Rose, 1884, quoted from Loison. One patient was a man forty-six years old who was injured by a carriage wheel passing over the chest. He became unconscious and expectorated blood. Two ribs were fractured. On the fourth day after the accident the patient died, and at autopsy a wound of the left ventricular wall was found. The wound was situated on the anterior surface of the ventricle and did not penetrate the cavity of the heart. There was also a small perforation of the pericardium, and the left lung was lacerated. The other patient was a man thirty-four years old who fell from a height of 14 meters. This patient became unconscious and died several hours after the accident. At autopsy a wound of the left ventricle was found. It did not penetrate into the cavity of the ventricle. The pericardium and the lung were lacerated.

CASE 8.—Potain, 1892. A man, forty years old, was struck over the third rib on the left by the shaft of a wagon. The patient became unconscious for a few minutes after the accident. He complained of pain where he was struck. One month after the accident he had palpitation of the heart, dyspnea on exertion, an irregular pulse, some enlargement of the heart, and a presystolic murmur. The patient died thirteen months after the accident. The examination showed an aneurysm at the apex of the heart, some dilatation of the conus arteriosus, and chronic myocarditis.

CASE 9.—Thiem, quoted from Erekclentz, 1910. This patient was a male who was kicked on the left side of the chest by a horse. For a period of two weeks following the accident the patient suffered with a feeling of substernal oppression and impending death. He also had sharp pain radiating down the left arm. Fifteen months later he died in an anginal seizure. The examination showed evidence of "old hemorrhages" in the interventricular septum.

CASE 10.—Vaquez, 1924. This patient received a violent blow in the region of the base of the heart by a carriage pole. Death occurred several months later, and an aneurysm in the region of the conus arteriosus was found.

CASE 11.—Joachim and Mays, 1927. This patient was a male, twenty-five years old. At the age of twelve years he had been run over by a wagon, and several ribs on his left side were fractured. At the age of twenty-three years he began to have severe attacks of paroxysmal tachycardia with a cardiac rate of 170 to 200 per minute. These attacks lasted for periods varying from ten minutes to one week and were accompanied by cyanosis, pulmonary edema, and congestion of the liver. He died suddenly at the age of twenty-five years. The autopsy showed an aneurysm of the left ventricle on the anterior wall near the apex. The myocardium at the base of the aneurysm was atrophic.

GROUP III. PATIENTS WHO DIED OF RUPTURE OF THE HEART

This group consists of 152 cases of cardiac rupture. The diagnosis was established by necropsy. An analysis of these cases showed that rupture of a cardiac chamber occurred in one of three ways.

- I. Bursting of the heart by compressing it between the sternum and vertebrae much as a toy balloon can be compressed in one's hand. It would seem that this compression would be more destructive if it were applied at the moment when the heart is filled with blood and is beginning to contract as at the end of diastole and at the beginning of systole. It would also seem that the compression would be more destructive if it were applied from the base of the heart toward the apex, thus preventing the blood from leaving the heart through the great vessels. Another factor in this type of injury is the marked friability of living cardiac muscle to abnormal forces. It is easily cracked and broken, and it would seem that the myocardium would break open if the heart were flattened out against the vertebrae even though it were empty and relaxed.
- II. Contusion of the heart with subsequent softening of the area of contusion (Howat, Kugel, O'Neill). Rupture takes place hours, days, weeks or months later. The intracardiac pressure is increased by physical exertion, and the bruised myocardium blows out when the patient exerts himself.
- III. Increased intracardiac pressure. This may be brought about by the application of forces directly to the heart as already referred to (Stephens, Ferris, Peacock), or it may be produced by the application of indirect forces as by sudden compression of the legs and abdomen (Kellert, Saphir).

That the heart and pericardium can be ruptured by the sudden application of a compression force limited to the abdomen and lower extremities seems to be impossible on a priori considerations. Nevertheless, Kellert reported the case of a man who was engaged in digging in a sand bank when suddenly the sand bank caved in and he was engulfed up to his waist. When he was dug out, he was dead. A laceration 5 cm. in length extended through the interventricular septum and opened both ventricular cavities. The endocardium of the right auricle was lacerated. The pericardium was ruptured. Microscopically there was some fatty infiltration of the right ventricular wall, vacuolization of the muscle fibers, and an occasional area of fibrosis. According to Kellert, "There are two possibilities in explanation of the lesion in the present instance. First, that the weight of the falling earth which, being soft and adaptable, caused equal pressure over the chest resulting in great compression and bursting of the heart, very much as though a rubber bag distended with fluid were compressed at its middle. To obtain such an effect without fracture of the sternum or ribs seems very unlikely. [However, Kellert stated that the patient was engulfed up to the waist.] The second and more probable explanation is that of hydraulic pressure. The large quantity of sandy soil exerted such great pressure over the lower half of the body as to drive most of the blood out of the vessels. This produced sudden overdilatation of the heart, which was probably dilated as a result of physical exertion, with consequent rupture at several points. That the force was a great one is indicated by the ruptured pericardium and hemorrhages in the lung. The pathologic changes in the heart, though not very marked, undoubtedly contributed to the severity of the injury."

Saphir reported the case of a boy, four years old, who was run over by a motor truck. The thoracic wall showed no evidence of injury. The pericardial cavity contained about 300 c.c. of blood. The left ventricular wall was ruptured for a distance of 6.5 cm. The myocardium showed no evidence of disease. The pelvis was fractured. Saphir stated: "While blows to the chest cannot be excluded, we saw no evidence of injury to the chest wall. Therefore the most probable explanation is that the rupture of the heart is dependent on the trauma of which the greatest force was exerted in the region of the right pelvis."

Stephens briefly recorded an example of rupture of the heart as follows: "A well-built lad, aged sixteen, was standing near a crane from which was suspended a heavy steel tube. As the tube was lowered it pressed against his chest and abdomen; he then stepped back a few paces and fell down, dead. Post-mortem examination showed the intrapericardial pressure was atmospheric, and on opening the sac it was found to be full of blood. In the right auricle was a tear one

inch long. Was this due to the back pressure caused by the tube pressing on his abdomen?"

Whether the heart can be injured by such indirect forces could not be answered by any experimental work that we were able to find. Accordingly, we carried out some experiments in which pressure was suddenly applied to the legs and abdomen and the compression effect upon the heart was studied. In these experiments we found that acute cardiac dilatation and failure could be produced, but in none of the experiments was the heart actually ruptured. Small hemorrhages in the epicardium and myocardium were not uncommon. The right auricular pressure showed a marked rise when the legs and abdomen were compressed, and it is probable that under certain circumstances actual rupture takes place in this way.

In the 152 cases of cardiac rupture that we analyzed, the way in which the trauma occurred was mentioned in 105 instances. In 38 instances the patient was run over by a wagon, automobile, or train; in 22 the patient was crushed between two objects, such as a wagon and a wall or two railroad cars; in 17 the patient was injured by a direct blow over the chest as by a club or a fist; in 12 the patient was struck by a falling object; in 8 the patient was kicked on the chest by a horse; in 3 the patient was injured in an explosion; in 2 the injury was sustained from a bullet striking against the sternum; in 1 the injury was sustained in a fall; in 1 the injury was sustained by the patient having been jumped upon by playmates, and in 1 the heart was ruptured when the patient was engulfed in a sand bank.

The largest group of cases (29) consisted of young men between the second and third decades of life. The second largest group of cases (22) consisted of boys between the first and second decades. In the entire group there were 113 males, 12 females, and 21 cases in which the sex was not mentioned.

It is interesting that the four cardiac chambers seem to be equally vulnerable to rupture. The right auricle was ruptured in 36, the left auricle in 30, the right ventricle in 31, the left ventricle in 37, and more than one chamber was ruptured in 13 cases. The interventricular septum was opened in 11 cases, and the interauricular septum was perforated in 1 instance.

It is also interesting to note that in 58 of the 152 cases it was specifically stated that the ribs or sternum, or both, were fractured; and in 88 cases either no mention of associated fractures was made or it was stated that there were no fractures of the thoracic cage. It should be emphasized that the heart can be ruptured by compressive or contusive forces without producing any fractures of the thoracic wall. One would expect this statement to apply especially to those cases in which the chest wall was pliable as in children and women

and men of frail build, but the heart can be ruptured in well-developed men without accompanying fracture of the chest wall.

The most frequent cause of death in this group of cardiac ruptures was neither the injury to the heart per se nor exsanguination. In 76 of the 152 cases of cardiac rupture the pericardium was distended with blood and the cause of death was hemocardiac tamponade. In 23 cases an extensive hemothorax was found. In 15 cases the injuries were extensive and involved other vital parts, and death was instantaneous. In 7 cases death was due to cardiac insufficiency. Two patients died with purulent pericarditis, one had pneumonia and one had pulmonary edema. In 21 cases the report was incomplete and the cause of death could not be determined.

These cases of cardiac rupture resulting from nonpenetrating trauma were analyzed in reference to their clinical manifestations and treatment. Obviously those cases in which death occurred immediately can be excluded from this analysis. They showed the signs of increased intrapericardial pressure or exsanguination into the thoracic cavity or injury to other vital organs. In 47 cases death occurred immediately after the accident, and in 42 cases the interval was not mentioned, but undoubtedly in most instances it was of brief duration. Thus any form of operative treatment was precluded by the time factor alone in 89 of the 152 cases. Out of the remainder of the group we selected those cases in which death did not occur within forty-five minutes or an hour after the accident. The second requirement for a case to be placed in this group was that the injury to the heart was not so extensive but that it might have been possible to repair it at operation. This special group consisted of 30 cases. It is an interesting group to analyze because it presents opportunities for treatment that were not utilized. Inasmuch as operation was not attempted in any of these cases, the group assumes sufficient importance to present it in tabular form, Table I.

If surgery has something to offer in this group of cases, the questions arise as to how the diagnosis can be made, which cases should be selected for operation, and what should be done at operation.

It is apparent from Table I that most patients had a short clinical course. Eighteen died within nine hours after the accident. If the patient survived the first nine hours, his chances of living through the first week were somewhat better than his chances of going through the second week. A possible explanation for this is that the area of contusion is weaker or softer during the second week than it is during the first week and that rupture is more prone to take place at that time. After the second week it would seem that the area of contusion becomes stronger because of the development of scar tissue. In the patients who survived the two-week period we find the duration of life being 30, 39, 49, and 60 days after the accident. Table I also

TABLE I
CASES OF CARDIAC RUPTURE POSSESSING SURGICAL POSSIBILITIES

NAME OF AUTHOR	SEX AND AGE OF PATIENT	TYPE OF INJURY	PATHOLOGY	MECHANISM OF RUPTURE	SYMPTOMATOLOGY	RESULTS
Bérard 1826	Male, young	Fell from a window.	Tear in left auricle. Much blood in pericardial cavity.	Not given.	Not given.	Death 2½ hr. later.
Lees 1837	Male, a brewer	Fell under a dray which passed over his chest.	Rupture of right auricle. Fracture of fifth rib. Blood in pericardial cavity.	Compression of chest.	Pain in chest, weakness. Drove horse for 1 hr., then walked into hospital.	Death 1 hr. later.
South 1839	Male	Run over.	Tear in heart at apex. Fracture of sternum and 2 ribs. Blood in pericardial cavity.	Fifth rib pierced the heart.	Not given. Walked 100 paces.	Death 9 hr. later.
Fenner 1846	Male, 30 yr.	Fell from a window on fourth story to pavement.	Rupture into left auricle, between mouths of pulmonary veins. Fracture right thigh.	Not given.	Prostrate, pulseless, cold. Pain in right shoulder, vomited.	Death 28½ hr. later.
Hewett 1847	Male, 29 yr.	Fell from a ladder.	Rupture of anterior wall of left auricle 0.5 in. long. Pericardium distended with blood.	Not given.	Cyanotic, cold, pulseless, pain in chest.	Death 2 hr. later.
Howett 1847	Male, middle age	Thrown from a cart, probably run over by it.	Rupture of left auricle and tear in pulmonary artery. Pericardium filled with blood.	Not given.	Collapse.	Death 4 hr. later.
Stanley 1850	Male, 38 yr.	Large iron plate fell on left leg.	Tear in endocardium of right auricle. Small tear into cavity of left auricle.	Not given.	Pulse feeble. Sepsis of leg.	Death 12 days later.

TABLE I—CONT'D

NAME OF AUTHOR	SEX AND AGE OF PATIENT	TYPE OF INJURY	PATHOLOGY	MECHANISM OF RUPTURE	SYMPTOMATOLOGY	RESULTS
Macleod 1858	Male, soldier	Hit by round shot on breast plate.	Small rupture of left ventricle. Pericardium contained 2 oz. of blood.	Not given.	Walked to rear. Acute pain in region of heart.	Death 72 hr. later.
Gregson 1859	Male, 38 yr.	Piece of iron fell on head.	Rent in anterior aspect of right auricle. Pericardium filled with blood.	Not given.	Headache.	Death 2 months later.
Sprakeling 1873	Male, 45 yr.	Knocked down by butcher's cart.	Laceration of left auricle. Pericardium filled with blood.	Not given.	Shock, soreness over injury. Heaving chest.	Death 8 hr. later.
Cleghorn 1873	Male, 28 yr.	Struck by lathe on left breast.	Rupture of apex entering left ventricle. Pericardium filled with blood.	Heart supposedly contracted and in contact with chest wall when blow was struck.	No external signs of violence.	Death 2 hr. later.
Heydenreich 1880	Male, 47 yr.	Chest caught between locomotive and stationary object.	Tear 3 cm. long into right auricle. 300 c.c. of blood in pericardial cavity. Fracture of sternum.	Severe compression of chest.	Loss of consciousness.	Death in 2½ hr.
Christiani 1889	Male	Not known.	Nonpenetrating wound of heart.	Wound which perforated after 39 days during violent exercise.	Not given.	Death in 39 days.
Hutchinson 1894	Male, 59 yr.	Kicked by a horse.	Tear into right ventricle, ¾ in. Rent in pericardium and blood in pleural cavity.	Direct violence.	Collapse, pain in cardiac region, pulse slow, regular, low blood pressure.	Death in 3¾ hr.

TABLE I—CONT'D

NAME OF AUTHOR	SEX AND AGE OF PATIENT	TYPE OF INJURY	PATHOLOGY	MECHANISM OF RUPTURE	SYMPTOMATOLOGY	RESULTS
Webersberger 1894	Male	Kicked by a horse.	Rupture 1 cm. long in wall of right atrium. 750 c.c. of blood in pericardial cavity.	Direct violence.	Vomiting, collapse, shock, pain in precordium. Not able to hear heart sounds.	Death in 1½ hr.
Bennett 1895	Male, young	Explosion of bomb.	Rupture left ventricle. Pericardium distended with blood. Wound in branch of left coronary artery. Fractured ribs.	Direct violence.	Collapse, masked heart sounds.	Death in 2½ hr.
Robertson 1897	Male, 49 yr.	Fell from open door of a railroad carriage.	Laceration of left auricle. Pericardium distended with blood clot. Normal heart muscle.	Violent impact of left shoulder. Direct violence.	Walked to work 200-300 yd. Sudden collapse.	Death in ¾ hr.
Groom 1897	Male, 16 yr.	Accident with runaway pony. Struck chest against a fish-trap.	Hole the size of a little finger in left ventricle. Pericardium filled with blood.	Incomplete tear of myocardium. Aneurysm which broke suddenly.	In bed 5 days, weak, sudden collapse.	Death in 1 month.
Gibbons 1897	Male, 30 yr.	Struck across chest with bamboo stick.	Small rupture in right ventricle. Pericardium distended with blood.	Direct violence.	Pain in left side. In hospital.	Death in 3 hr.
Newton 1898	Male, 28 yr.	Fell on handlebar of bicycle.	Tear in apex of right ventricle. Pericardium contained 10 oz. blood. Fracture of left 6th costal cartilage.	Direct violence.	Pain in left side. Collapse, failing pulse.	Death in 1½ hr.

TABLE I—Cont'd

NAME OF AUTHOR	SEX AND AGE OF PATIENT	TYPE OF INJURY	PATHOLOGY	MECHANISM OF RUPTURE	SYMPTOMATOLOGY	RESULTS
Ebbinghaus 1902	Male, 12 yr.	Fell from window six floors to the ground.	Rupture into the left ventricle. Pericardium distended with blood. Myocardium softened about rupture.	Contusion of myocardium with subsequent softening.	Unconscious. Cardiac dullness normal. No symptoms after 3 days until sudden collapse 9 days later.	Death 9 days later.
Kugel 1909	Male, 14 yr.	Struck by a heavy bale of goods.	Rupture of right atrium. 500 c.c. of blood in the pericardial cavity.	Forceful rupture of heart. Question of strain from heavy lifting.	Coma, immediate collapse, pulseless, cold and clammy.	Death 42 hr. later.
Corin 1911	Male, 63 yr.	Crushed by a wagon loaded with coal.	Transverse tear into left ventricle. Pericardium distended with blood.	Vertebral column acted as a wedge. Left heart distended at time of compression of thorax.	Examination negative, told to return to work. Sudden collapse.	Death 5-6 hr. later.
O'Neill 1914	Male, 9 yr.	Knocked down and jumped on by boys while playing.	Perforation 3 mm. long in right auricle. 700 c.c. of blood in pericardial cavity.	Rupture first, then sealed off and then broke loose again.	Pain in left side. In bed for 2 days. Sudden collapse 5 days later. Death 1 hr. after collapse.	Death 7 days later.
Kennedy 1914	Female, 60 yr.	Knocked down by a cart shaft which struck right mammary region.	Two small ruptures into left ventricle. 10 oz. of fluid in pericardial cavity. Fracture of sternum and ribs.	Rupture by bursting.	Not given.	Death 1 hr. later.

TABLE I—CONT'D

NAME OF AUTHOR	SEX AND AGE OF PATIENT	TYPE OF INJURY	PATHOLOGY	MECHANISM OF RUPTURE	SYMPTOMATOLOGY	RESULTS
Turner & Gould 1917	Male, 47 yr.	Fell 20 ft. from ship against a buoy.	Small tear in anterior wall of right ventricle. Fracture of sternum. 15 oz. of blood in pericardial cavity.	Rupture at time of accident, clot which later gave way. Direct violence.	Unconscious, shock. Heart sounds distant. Conscious at 5 hours. Sudden collapse.	Death 7 hr. later.
Howatt 1920	Male, 68 yr.	Chest squeezed by truck against an iron pipe.	Left ventricle bruised in 5 places, apex ruptured. Pericardial cavity full of blood.	Bruise of cardiac muscle which ruptured later.	In bed 2 weeks. Resumed work for 3 weeks. Pain in chest on exertion. Sudden collapse.	Death 7 weeks later.
Reid 1922	Female, 5 yr.	Fell from porch two feet, striking corner of cement step	Rupture of left auricle. Pericardium filled with blood. Blood in pleural cavity and in left lung.	Question of bruise of cardiac muscle and later rupture.	Examination negative at time of injury. Sudden collapse seven days later.	Death 7 days later.
Tuohy & Berdez 1926	Male, 11 yr.	Struck by an automobile.	Small perforation at the apex of left ventricle. Pericardium distended with blood.	Compression of thorax.	Shock, pulse rapid, heart sounds scarcely audible. 2 hours later heart sounds more distant. Pulse slow.	Death 3 hr. later.
Tuohy & Berdez 1926	Male, 63 yr.	Automobile accident, thrown against steering wheel.	Rupture, one inch long, in wall of left ventricle. Pericardial cavity full of blood.	Bruise of myocardium. Increased blood pressure while laughing caused rupture.	Distress in chest, frequent vomiting, sudden collapse.	Death 2 weeks later.

shows that the cause of death in the entire group of cases with one exception (exsanguination) was increased intrapericardial pressure. Several cases showed some contusion of the myocardium in addition to the hemopericardium. In this entire group of cases the opening into the cardiac chamber was not extensive, and the bruising of the myocardium was slight or absent.

The most prominent group of clinical manifestations in these cases was the sudden collapse. The patient may complain of precordial pain, or the pain may be referred to the heart to the left side or to the shoulder. The pulse may be slow or rapid, but as the pressure in the pericardial cavity increases, the pulse becomes feeble. Vomiting and headache may be present. The patient may be restless, he may show great anxiety and may develop air hunger. The vasomotor center makes a heroic effort to maintain an adequate arterial pressure. It is able to do this even when the output of the heart is reduced 50 per cent of the normal (Beck and Isaac). A point is finally reached when the blood in the venous reservoirs can no longer break through the intrapericardial barrier. The skin becomes cold and blanched, some cyanosis may be present, but pallor is more conspicuous than cyanosis, the blood pressure falls, and unconsciousness supervenes. The cardiac sounds become distant and may not be audible. There may or may not be any demonstrable increase in the extent of the cardiopericardial dullness. To take an x-ray picture of the heart may be a waste of valuable time if it should delay an urgent operation. The venous pressure is a good index of the intrapericardial pressure. The height to which the venous pressure rises in cases of cardiac rupture or in stab wounds of the heart cannot be given because such determinations have not been made. Such data would be valuable because the venous pressure might be a guide as to when operation is indicated. Experimentally when the intrapericardial pressure is acutely elevated, the heart is brought to a standstill when the venous pressure is elevated 13 to 15 cm. of physiological solution of sodium chloride. However, if there is active and continuous bleeding in the pericardial cavity, the condition is one of great urgency, and time does not permit the determination of the venous pressure. A definite diagnosis of bleeding into the pericardial cavity can be made by tapping the pericardial cavity with a needle. Indeed, it might be possible by removing some of the blood in this way to keep the patient alive until the operation can be done.

EXPERIMENTS

In order to study the effect of contusions of the heart, we carried out a series of twenty-five experiments the results of which we herewith report. Male dogs were selected weighing from 17 to 25 kilograms. These were trained to lie quietly so that electrocardiograms

could be taken. The size of the heart was determined by x-ray examination. Ether anesthesia was used. The heart was exposed under aseptic precautions from either the left or the right side. The pericardium was incised. The cardiac rate was determined. In five experiments the left femoral artery and the left jugular vein were cannulated and connected to a mercury manometer and a water manometer respectively. The myocardium was then bruised. Usually this was done by striking the myocardium with a metal dilator weighing 40 grams. Repeated strokes with the dilator were applied to a localized area over either the right or the left ventricle. In a few of the experiments hard blows were given to the myocardium with a considerably heavier instrument. Three deaths occurred while the heart was being traumatized, one from rupture and two from ventricular fibrillation. In one experiment 10 c.c. of blood and in another experiment 20 c.c. of blood were injected into the interventricular septum. After these various forms of trauma were applied to the heart, the pericardium was sutured and the wound in the thoracic wall was closed.

Observations: The immediate response of the heart to this trauma was an increase in the pulse rate. The tachycardia frequently became so rapid that the rate could scarcely be counted. A rate of 160 to 180 per minute was not unusual. Occasionally the pulse rate became somewhat slower, and in a few instances the rate decreased and then became rapid. The arterial pressure showed wide fluctuations at the time the myocardium was being traumatized. The pressure momentarily dipped down from about 100 or 120 mm. Hg to 40 or 50 mm. Hg, and then after the application of trauma was discontinued, the arterial pressure usually ran along 20 to 50 mm. Hg below the normal level. Sometimes the arterial pressure made a complete recovery to the normal level. The venous pressure rose 10 to 15 cm. of water while the myocardium was being traumatized, but after the application of trauma was discontinued, the venous pressure returned to normal. The myocardium became swollen and discolored after it was bruised. This was due to extravasation of blood into the myocardium. It was surprising to us to see the amount of trauma that the myocardium could tolerate. Not infrequently the myocardium was bruised to such a degree that one would expect softening and rupture to take place. Rupture of the heart did not occur in any of the survival experiments. In two experiments the heart went into ventricular fibrillation at the time the trauma was applied. In these experiments the heart did not recover its normal rhythm after it began to fibrillate, and death occurred. In each of these experiments an extensive extravasation of blood was found in the interventricular septum. In one experiment death occurred from cardiac failure a few hours after the operation was completed. In the survival experiments, after the

effects of the anesthetic wore off, the pulse rate remained rapid, and the cardiac sounds were faint and distant. In several of the experiments the cardiac sounds could not be heard for several days after the operation; in others the cardiac sounds had a rapid "tick-tick" quality. This was quite characteristic and helped us later to recognize clinically a cardiac contusion in a human patient before death. Even though the cardiac sounds were scarcely audible and the pulse rate was rapid, the dog appeared like any other dog when one approached his cage. He stood up and showed the usual activity, but he was not allowed to exercise, and we cannot make a statement as to how the dog could tolerate activity after a contusion of the heart was produced. Undoubtedly the circulatory reserve was decreased. One dog died of cardiac failure forty-eight hours after the experiment. At necropsy

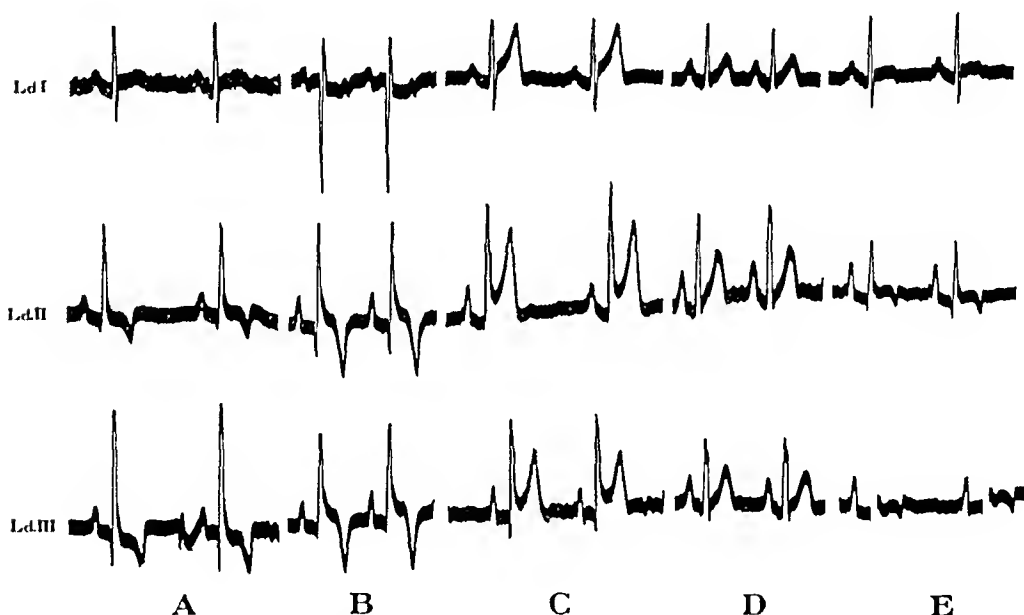


Fig. 1.—Dog 120. A, Normal control June 4, 1932. B, After injection of 10 c.c. of blood into interventricular septum June 11. Deep Q in Lead I; S-T in Leads II and III slightly everted. T in Lead I diphasic; sharply inverted T in Leads II and III. C, June 18, S-T in Leads I, II and III elevated with sharply everted T-waves of increased amplitude. D, June 24, T large in amplitude in all leads. E, July 13, T in Leads II and III diphasic.

50 c.c. of blood-stained fluid were found in the pericardial cavity, and the heart and the parietal pericardium were adherent at the site of the contusion.

The size and contour of the heart were determined by x-ray pictures standardized as to distances of plate and target from the heart so that comparisons of the shadows could be made. In three-fourths of the experiments cardiac dilatation was demonstrated and the cardiopericardial shadow had an indistinct boundary. This enlargement usually persisted for two or three weeks, when it returned to the normal size, and the outline of the shadow again became distinct. In about one-half of the experiments a blood-stained pericardial ef-

fusion was demonstrable either by tapping the pericardial cavity or by x-ray examination. Occasionally the cardiopericardial shadow remained somewhat enlarged for a month after the trauma. In about

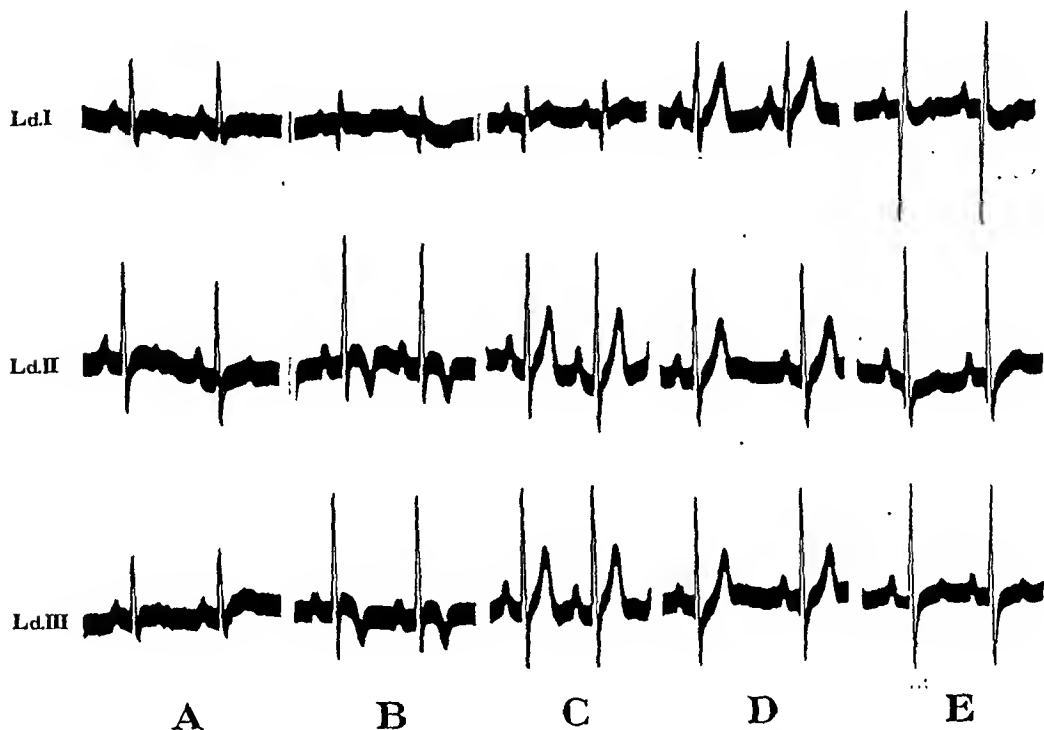


Fig. 2.—Dog 73. *A*, Normal control April 24, 1932. *B*, After 14 blows to left ventricle May 14. S-T in Leads I and II slightly everted, T in Leads I, II and III inverted with sharp angulation, Q in Lead III appeared. *C*, May 21, Q in Lead I; T upright in all leads (large amplitude in Leads II and III). *D*, May 28, T upright in all leads with large amplitude. *E*, June 16, Q in Lead I deep; diphasic T in Lead I; T in Leads II and III upright but of low amplitude.



Fig. 3.—Dog 76. *A*, Normal control April 22, 1932. *B*, After 50 blows to left ventricle near apex May 10. QRS of low amplitude; S-T in Leads II and III slightly everted; T in Leads II and III inverted. *C*, May 14, QRS of greater amplitude; T upright in all leads. *D*, May 21, T in Leads I and II increased in amplitude. T in Leads II and III diphasic. *E*, June 4, QRS complex shows increase in amplitude in all leads. T in Lead I upright, T in Leads II and III diphasic. *F*, June 16, deep Q in Lead I, T inverted in Leads I and II, diphasic in Lead III.

one-fourth of the experiments the size and contour of the cardiopericardial shadow did not change from the normal. In clinical cases we believe that if a blood-stained effusion can be demonstrated by aspira-

tion of the pericardial cavity after an injury, one can consider this as evidence in favor of a cardiac contusion.

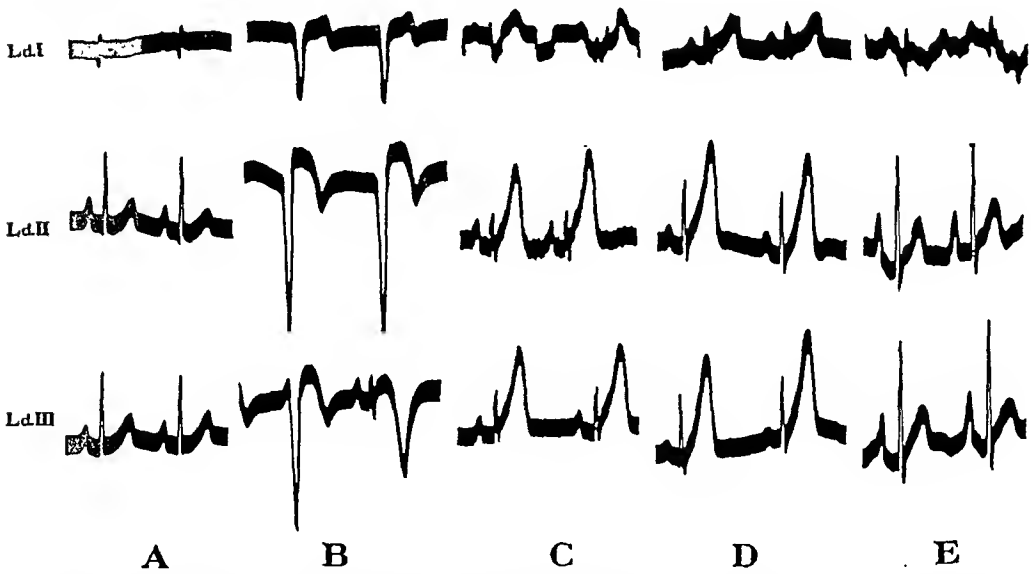


Fig. 4.—Dog 110. *A*, Normal control May 10, 1932. *B*, After 24 blows to wide area of left ventricle May 14. Ventricular tachycardia. In Lead III one normal beat is seen. S-T in Lead III is slightly everted, and T in Lead III is sharply inverted. *C*, May 21, deep S in Lead I; QRS low amplitude in all leads; T increased in amplitude in all leads. *D*, May 28, QRS back to normal amplitude; T-waves large amplitude in all leads. *E*, June 16, Q-wave appears in Lead I; T inverted in Lead I; T lower in amplitude in Leads II and III.

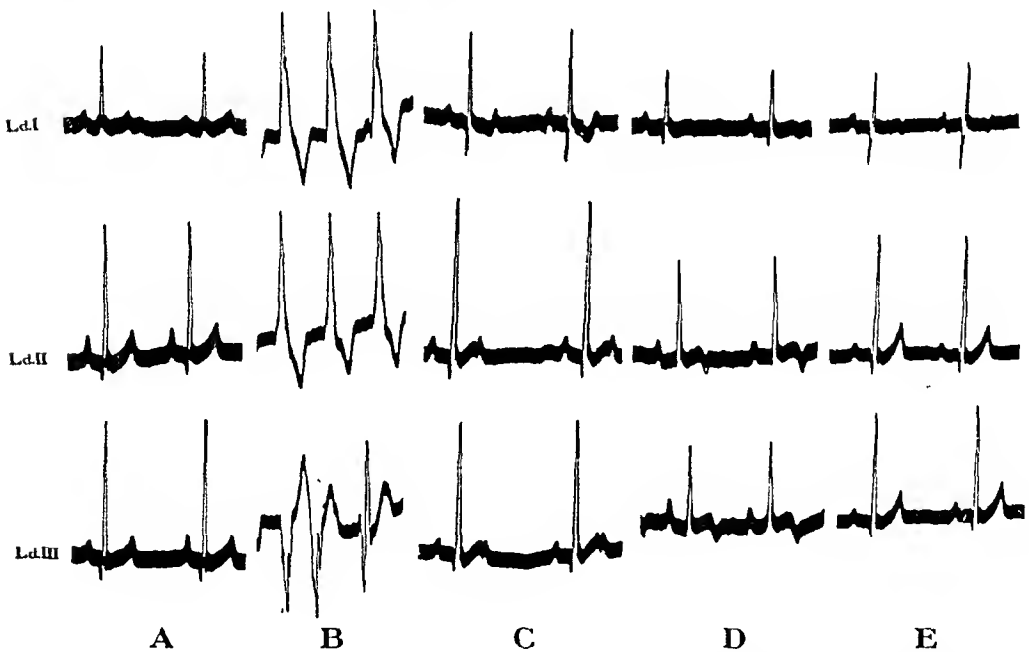


Fig. 5.—Dog 124. *A*, Normal control June 4, 1932. *B*, After 25 blows to right ventricle June 11. Ventricular tachycardia. *C*, June 18, Q in Lead I appears; T in Lead I diphasic; T notched in Leads II and III. *D*, June 24, T in Leads II and III inverted; slight eversion of S-T in Leads II and III. *E*, July 13, deep Q in Lead I.

The cardiac sounds usually remained faint and distant for a period of a week or ten days after the operation. The pulse rate also remained elevated for about the same period of time. Frequently the

normal sinus arrhythmia was lost for two to three weeks, but when the rate became slower it again appeared.

The electrocardiograms in these experiments showed a variety of alterations from the normal. These were analyzed by Dr. Harold Feil and are illustrated in Figs. 1, 2, 3, 4, and 5, and in Table II. The most frequent variation from the normal was the production of large T-waves and alterations in the Q-wave. Frequently there was a high take-off of the T-wave; sometimes the T was inverted. Slurring and

TABLE II

DOG	INJURY	EARLY EFFECTS	LATER EFFECTS
32-120	10 c.c. blood injected into interventricular septum. Post mortem: heart negative.	Deep Q. High take-off of S-T _{2,3} deeply inverted T _{1,2,3} (48 hr.). High take-off Leads I, II, III. Very high T _{1,2,3} .	15 days: T _{2,3} very tall. 32 days: Back to normal.
32-73	14 hard blows to left ventricle near apex. Post mortem: Scar over injury.	48 hr.: Deep Q. T _{1,2,3} inverted. 9 days: Tall T _{2,3} .	16 days: Tall T _{1,2,3} . 35 days: Deep Q. T back to normal.
32-76	50 severe blows to apex left ventricle. Post mortem: adhesions between pericardial layers over injury.	Low voltage, slurring QRS in Leads I, II, III.	11 days: Large T _{1,2,3} . 24 days: T ₂ sharply negative. 36 days: Deep Q.
32-110	24 blows over left ventricle. Post mortem: numerous adhesions over epicardium.	2 days: Nodal rhythm and intraventricular block (2-1). High take-off S-T in Leads I, II, III. 9 days: High take-off S-T in Leads I, II, III. Very large T _{2,3} . QRS low amplitude.	16 days: Large T _{1,2,3} . 34 days: Deep Q ₁ . T _{2,3} high.
32-124	25 blows to right ventricle. Post mortem: Heart negative.	24 hr. Ventricular tachycardia. 8 days: T ₁ inverted.	14 days: T _{1,2} inverted. 33 days: Deep Q ₁ .

notching of the QRS complex occurred frequently. These deviations from the normal electrocardiogram in great part had disappeared after about one month, but some of these alterations persisted for a longer period of time. It is interesting to note that the electrocardiogram obtained in the experiments in which blood was injected into the interventricular septum was somewhat similar to the electrocardiogram obtained in the experiments in which the myocardium was bruised. This, together with the fact that most of the electrocardiographic changes disappeared after a few weeks, would indicate that these alterations were largely due to hemorrhage. The changes in the

electrocardiogram are somewhat similar to the electrocardiographic changes accompanying tamponade, or arterial occlusion with myocardial degeneration due either to arterial or to arteriolar sclerosis.

The animals were killed with chloroform narcosis two or three months after operation. All of them appeared to be in good health before they were sacrificed. It was amazing to us to see how well the myocardial damage was repaired. In three of the specimens there was no trace of the injury to the myocardium, no adhesions and no

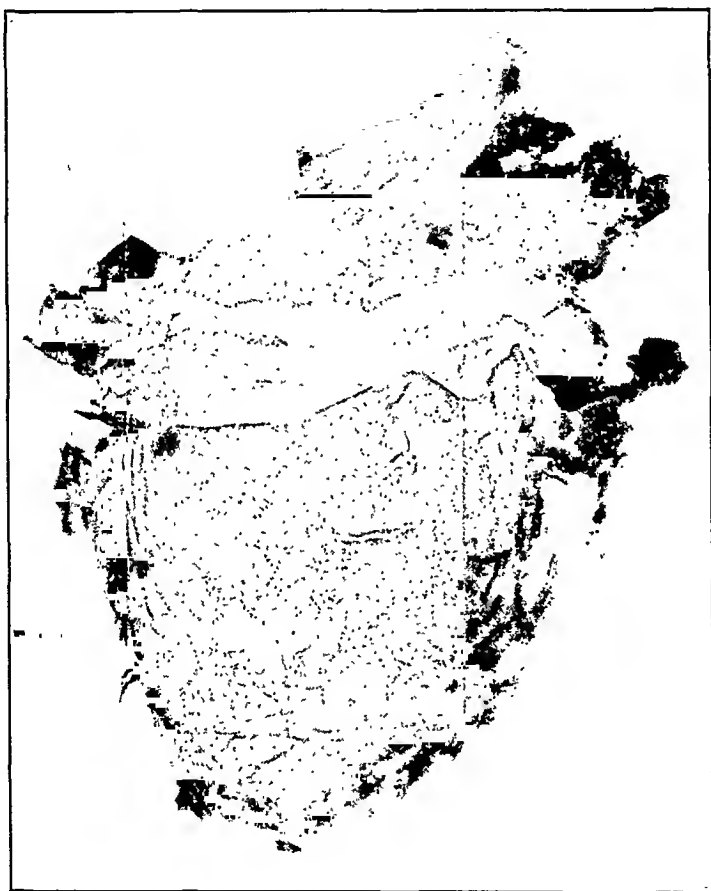


Fig. 6.—The heart was exposed at operation, and the myocardium was injured by applying a contusive type of trauma. The damage was repaired by the development of scar tissue at the site of the contusion. The myocardial scar can be seen near the apex of the heart. The entire epicardial surface in this specimen was adherent to the parietal pericardium. In some cases the parietal pericardium seals over the contusion and protects it from rupture.

demonstrable scar tissue formation in the myocardium. In the remainder of the group, consisting of 14 specimens, adhesions between parietal pericardium and epicardium were found. In nine of these the adhesions were limited to the area of myocardium that was bruised; while in the remainder adhesions were generalized but more marked at the site of the injury (Fig. 6). In some of the specimens the adhesions were easily torn apart, but in others the scar penetrated the myocardium. In none of the experiments was the entire thickness

of myocardium penetrated by scar tissue. The scarred area appeared firm and strong, and in no experiment was there any tendency to the formation of an aneurysm of the myocardium. Microscopically the scar could be traced into the myocardium, but nowhere did it replace the entire thickness of the ventricular wall. It was generally confined to the epicardial region. Lymphocytes were found infiltrating the newly formed fibrous tissue and extending also into the subjacent myocardium. Also some small blood vessels were seen in the fibrous tissue.

DISCUSSION

When we began to study this subject of nonpenetrating cardiac trauma, we shared the opinion which we believe is general, namely, that such wounds are exceedingly rare and that so far as clinical manifestations and treatment are concerned the subject is of comparatively little importance. This opinion was changed as the data were assembled. The entire literature was not available, but the number of cases that we were able to analyze was large enough to give an accurate idea of the relative incidence of the various types of such traumas. The important fact brought out by this analysis was that the number of cases that terminated fatally was relatively very high, while the number of cases that recovered was relatively very low. In our analysis of 168 cases death occurred in 157. Of these 157 fatal cases rupture of the heart occurred in 152, or 96.8 per cent, and myocardial failure in 11, or 6.5 per cent. The diagnosis in the entire group of fatal cases was made by necropsy examination. Of the entire group of 168 cases only 12 survival cases were found. This was only 7.1 per cent of the total number. The diagnosis in this group was made on clinical grounds. If these figures can be considered as representative of the true ratio of incidence in cases of rupture, cardiac failure, and recovery, then it can be stated that when the heart receives a nonpenetrating wound, death almost always follows and recovery seldom occurs. Obviously this conclusion is wrong. In the experiments we found that the heart could tolerate a great amount of trauma and that rupture was a rare complication. Experimentally, recovery was the rule rather than the exception. We believe we can conclude from this data that the vast majority of nonpenetrating wounds of the heart are not recognized clinically. These patients recover and only the exceptional one dies of the trauma, showing at necropsy a rupture or a contusion of the myocardium. These exceptional cases find their way into the literature. The other cases in which death does not occur apparently do not receive the correct diagnosis and are not placed in the literature.

We hesitate to try to discuss the subject of diagnosis in this group of cases because the clinical criteria upon which the diagnosis might be based are not infallible. Each of two patients may have been

subjected to similar forms of trauma; both may develop similar clinical manifestations, and these in one may be due to a myocardial contusion and in the other to coronary disease. An accurate differentiation may be impossible. Mistakes can be made in either direction, but the point that we should like to make is that the rôle of trauma is too frequently overlooked. A patient who has been in good health, who receives either direct or indirect trauma to the chest, who then develops symptoms of circulatory embarrassment should, in our opinion, be considered as having sustained a cardiac injury unless other evidence points to a different diagnosis. The heart is not immune to trauma whether the trauma appear to be slight or serious, whether the symptoms be mild and transient or severe and permanent. Naturally an irregularity of the pulse, dyspnea, and anginal pain coming on immediately after an accident in a patient who had no cardiac symptoms previously causes the patient considerable concern and worry. In such cases a diagnosis of cardiac neurosis may be incorrect. Likewise anginal pain and electrocardiographic evidence of a myocardial infarct precipitated by an accident, such as a golf ball striking against the precordium,* are scarcely coincidences.

Although the literature on cardiac contusions consists largely of case reports, a general discussion of the subject is presented by Kahn and Kahn. For purposes of industrial compensation they presented what they considered compensation criteria. These are as follows:

"1. From a labor standpoint, the heart is healthy if a man is able for a long period of time to pursue his occupation without distress and without long periods of absence from work.

"2. If, following direct or indirect violence to the chest, signs of an intrathoracic cardiovascular lesion develop, which are incapacitating, they must be considered the result of an aggravation of a previously existing asymptomatic lesion, or the result of damage to a previously normal heart.

"3. As in heart strain, the time that elapses between the accident and the development of disabling symptoms is very short. There must be immediate pain with its concomitants—dyspnea, rapid irregular pulse, faintness, and cold sweat, and immediate partial or total disability, in order that causal or aggravating relationship be clearly established. Temporary improvement with return to usual or lighter work, followed by a recurrence of the condition, may occur. But in these cases the reappearance of the symptoms and signs should be attributed to the original injury."

We believe that we should make some comment upon the important medicolegal question concerning the interval of time between trauma and onset of symptoms. Kahn and Kahn are definite in their statement that pain, dyspnea, rapid irregular pulse, etc., should develop

*J. A. M. A. 101: 1503, 1933 (Queries and Minor Notes).

immediately after the accident in order to establish causal relationship between cardiac trauma and cardiac symptoms. As already pointed out, almost all cases of cardiac contusion in the literature are cases that terminated fatally. These patients sustained a serious degree of cardiac contusion, and in the cases of this group that were fully reported the symptoms did come on immediately after trauma. In some of the fatal cases the pulse was slow and not rapid. This is a point of difference with the statement by Kahn and Kahn. It is also supported by our experiments. In some of the fatal cases, even though symptoms appeared early, these symptoms gradually became worse over a period of hours, days, or weeks after the accident. In considering cases in which the trauma is less serious, cases in which recovery takes place, the material for analysis is so meager that we hesitate to make a definite statement concerning the possibility of an asymptomatic period after the accident. To support the possibility of a symptom-free period after trauma are the cases of Moullin and of Joachim and Mays. These cases are suggestive of a free period in that the one patient played football after the accident and the other developed paroxysmal tachycardia and an aneurysm of the myocardium years after the trauma. We also know that after a contusion has been inflicted upon the myocardium a process of change takes place in the myocardium. This consists of capillary hemorrhage, infiltration with leucocytes, edema, resolution, and finally scar tissue formation. These changes in the myocardium are progressive, and while their ultimate result is the formation of a scar, nevertheless rupture or an aneurysm may develop subsequently. These complications can produce latent symptoms. On the basis of such data we believe that the onset of symptoms may be somewhat delayed in certain cases of cardiac contusions. Further data are necessary to establish this point.

TREATMENT

The diagnosis of a cardiac contusion having been made, what course will the patient follow? There are several possibilities: (1) the symptoms may disappear hours or days after the accident, and the patient may remain well; (2) the symptoms may persist for years, and they may be accentuated by exercise; (3) the heart may fail hours or days after the accident; (4) the contusion may soften, and rupture may take place. Therapeutic measures can be taken to guard against myocardial failure and cardiac rupture. Obviously these measures consist of absolute rest and the use of morphine or other sedatives as necessary. The heart should be saved as much as possible. Any exertion should be avoided. Mild laxatives should be given, if necessary, to avoid straining at stool. Digitalis may be indicated for the tachycardia or auricular fibrillation. The contusion may rupture any

time during the first month, but most commonly the rupture, if it occurs, takes place during the second week.

According to our analysis of the cases in which rupture occurred, surgical intervention should be considered. When rupture occurs, the need for immediate operation is urgent. For that reason a surgeon should remain in constant attendance; the operating room should be in constant readiness so that the fleeting opportunity to suture the wound can be utilized. Up to the present time operation has not been attempted in any case of cardiac rupture. To Mansell Moullin belongs the credit of having evacuated bloody fluid from the pericardial cavity in a boy who had sustained a nonpenetrating form of trauma. Recovery took place, but the heart was not explored, and it was not determined whether a rupture was present. The hemorrhage in this case might have come from the myocardium or it might have been a hemorrhagic effusion, such as we observed in our experiments.

If there is any evidence of a pericardial effusion in these cases, tapping the pericardial cavity would seem to be advisable. The demonstration of bloody fluid is helpful in diagnosis, the removal of the fluid may relieve the circulation. In certain cases it might do as much good as operation and might make operation unnecessary.

If signs of increased intrapericardial pressure develop suddenly, indicating rupture, the operation must be done without any delay. What one would expect to do at the operation would depend upon the conditions found. After the mediastinum is opened, the tamponade would be relieved by opening the pericardium. Procedures to start the heart beating may be necessary. If the heart is beating, the problem of preventing hemorrhage is presented. The methods of controlling hemorrhage will not be presented here.* Sutures should be placed at the site of the hemorrhage. If the myocardium is extensively bruised and softened, grafts of pericardium should be placed on the area of contusion and securely sutured to the myocardium. Adhesions between pericardium and myocardium is Nature's way of treating such contusions, but these adhesions may not give a secure union, and in our experiments they were absent in over half the cases. It is not a far stretch of the imagination to apply this operation not only to these traumatic cases but also to those cases in which myocardial infarction due to coronary disease is present. Such a graft placed over an infarct should afford protection from rupture.

CASES OF RUPTURE OF HEART RESULTING FROM NONPENETRATING WOUNDS OF CHEST

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MECHANISM OF PAIN PRODUCTION IN ANGINA PECTORIS*†

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INTRODUCTION

DURING the past few years we have investigated several aspects of the problem of pain production in angina pectoris. The work dealt in part with patients having angina pectoris, in part with the production of pain in contracting skeletal muscles in normal persons, and in part with animal experimentation. In this report an attempt is made to summarize briefly the various deductions and conclusions derived from the foregoing studies.

The subject of angina pectoris is an old one, and the theories concerning the mechanism of its production are manifold. At the present time, however, the majority of workers have come to view ischemia of the heart as the most likely cause for angina pectoris. There is no need of reviewing the pertinent literature in view of the several excellent reviews already published among which the more recent are those of Keefer and Resnik¹ and Lewis.²

The evidence for the ischemic theory of angina pectoris has been derived from four sources: (1) that based on clinicopathological correlations; (2) that based on clinico-electrocardiographic correlations; (3) that dealing with observations on contracting ischemic skeletal muscles; and (4) that dealing with observations made on animals.

CLINICOPATHOLOGICAL CORRELATIONS

While the commonest pathological lesions found in patients with angina pectoris are coronary sclerosis and myocardial fibrosis, these lesions of the heart often occur without being associated with angina pectoris. Even in coronary thrombosis the dramatic clinical picture is sometimes absent (cf. Saphir, Priest, Hamburger and Katz³). It is not difficult to explain the occurrence of pain in the foregoing conditions on the basis of relative or absolute ischemia of the heart. It is much more difficult to account for the absence of pain when a similar degree of ischemia is present, unless some other factor or factors are concerned.

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CLINICO-ELECTROCARDIOGRAPHIC CORRELATIONS

A similar conclusion was reached from an analysis of clinico-electrocardiographic studies. In confirmation of the work of others we have found that bodily exercise and generalized anoxemia may precipitate attacks of angina pectoris in patients suffering from this disease, usually with alterations in the electrocardiogram similar to those in spontaneous attacks of angina pectoris. Similar electrocardiographic changes were produced in normal persons by these procedures without causing precordial pain and such electrocardiographic changes were found in patients with a history of angina pectoris following anoxemia or exercise even when unaccompanied by attacks of angina pectoris (cf. Katz, Hamburger and Lev,⁴ Katz, Hamburger and Schutz,⁵ and Katz and Landt⁶). These results also indicate that some other factor besides ischemia plays an important rôle in the production of angina pectoris.

OBSERVATIONS ON ANIMALS

A clue to the possible factors involved was derived from our animal experiments. In the course of an investigation of the pathways taken by the pain fibers in the dog we had occasion to repeat some of the experiments of Sutton and Lueth⁷ and were surprised to find that the responses recorded by these authors did not always occur (Katz, Mayne and Weinstein⁸). We were able to confirm the observations of previous workers that occlusion of the coronary vessels and the surrounding tissues in the unanesthetized dog gave rise to effective responses resembling an anginal attack. The response was similar to that obtained on compressing a superficial somatic sensory nerve except for the inability of the animal to locate the site of irritation. However, our results showed that the pain response was not due to the occlusion of the coronary artery but to stimulation of afferent pain fibers located in the nerve plexus surrounding the vessels. The evidence for this is:

(1) Occlusion of a carefully isolated strip of the coronary artery gave no response, but a definite response was obtained when the undissected coronary vessel was compressed above and below this point.

(2) Destruction of the nerve plexus surrounding the vessel with phenol-alcohol abolished the response to compression, but the response was still positive when a region above the phenolized area was stimulated.

(3) Complete preliminary occlusion of the carefully isolated coronary artery did not prevent a positive response to compression above or below this point.

(4) Pericardial "tamponade" following bleeding from a ruptured coronary artery caused syncope but no "anginal" response.

Positive responses occurred only when the region about the coronary vessels was compressed, the rest of the myocardium and epicardium

was found to be insensitive to pressure stimulation. As a result of this study it can be concluded that ischemia of the myocardium need be only one of many mechanisms operating on the nerve endings and nerve fibers surrounding the coronary vessels which can give rise to anginal attacks. It is conceivable that sudden rises in blood pressure could mechanically stimulate these nerve endings and give rise to pain attacks. Furthermore the direct action of the arteriosclerotic processes on the coronary vessels spreading to the adventitia and accompanied by periarterial changes could render the nerve endings within the walls at first hyperirritable and later, by destruction, insensitive to stimulation. Such changes would most certainly alter the pain response. Stimuli which would ordinarily be without effect on the pain endings might be effective when the nerve endings were hyperirritable. This may be the crux in the difference in response to the same stimulus in different patients. It must be further borne in mind that during the process of involvement of the nerve endings and also of the nerve fibers in the adventitia, the actual advance of this pathological process may by itself give rise to painful attacks as successive groups of fibers and endings are first stimulated and then destroyed. Myocardial infarction may operate in exactly this way on the nerve endings and nerve fibers present in the infarcted area.

It is not unlikely that the pain response obtained by Sutton and Lueth⁷ in probing the mouths of the coronary vessels might have been due to stimulation of this nerve plexus rich in pain fibers and not directly to the occlusion of the mouths of the coronary arteries. It is indeed possible that even sudden death, the result of ventricular fibrillation, could have been caused by reflex or direct nerve stimulation.

OBSERVATIONS ON CONTRACTING SKELETAL MUSCLES IN NORMAL PERSONS

The greatest support for the ischemic theory has come out of the work on human skeletal muscle. It has been known for a long time that continuous pain can be produced in contracting skeletal muscle when the muscle is rendered ischemic. The concept that it is due to spasms of the vessels has been definitely disproved by the work of Lewis, Pickering and Rothschild.⁹ The immediate factors responsible for the muscular pain have not been fully established. The pain which develops in contracting muscles during ischemia might be caused (1) by the direct or indirect action of the lack of oxygen which accompanies ischemia, (2) by the diminution of other materials normally supplied by the arterial blood, (3) by the incomplete mechanical removal of products of muscular metabolism which follows the retardation of the blood flow, or (4) by the combined action of several of these factors. The observations made in this laboratory on this phase may be sum-

marized as follows (Kissin,¹⁰ Perlow, Markle and Katz,¹¹ and Katz, Landt and Lindner¹²).

(1) Generalized anoxemia, without impeding the circulation to a limb or obstructing its venous flow, lessens the amount of exercise necessary to cause continuous pain in the contracting muscles. The amount of exercise needed to cause pain decreases progressively but not linearly as the generalized anoxemia is augmented.

(2) Obstructing the venous flow in an otherwise normal limb also decreases the amount of exercise needed to cause pain, and in proportion to the degree of stagnation produced.

(3) When the circulation is free and anoxemia is absent, increasing the rate of exercise decreases the amount of exercise required to cause pain.

(4) A preliminary period of complete ischemia before starting the exercise definitely lessens the amount of exercise required to cause pain.

(5) Continuing the ischemia of the limb after stopping the exercise short of the point at which previous tests have shown that pain will appear, will lead to the appearance of pain after a long lag. This lag was found to be from 20 to 80 times longer than the time at which pain would have appeared if the exercise had been continued—which is roughly of the order of magnitude of the ratio generally accepted to exist between the metabolism of resting and exercising muscle.

(6) The condition of the limb before the exercise is started determines the amount of exercise required to produce pain, there is thus a definite pre-pain stage.

(7) Elevating the CO_2 content in the blood contained in an ischemic limb lessens the amount of exercise necessary to produce pain.

(8) Alkalinization of the subject by large quantities of sodium bicarbonate definitely increases the amount of exercise required to produce pain.

(9) We have confirmed the observations of Laplace and Crane¹³ that fatigue, rather than unbearable pain, may, in some instances, make it impossible to further contract the muscles.

(10) We have obtained definite evidence that a substance formed during exercise of one group of muscles can pass the lungs and into another group of muscles, so that the amount of exercise required to cause pain is decreased in the latter.

From these observations we conclude that the stimulus for pain appears to consist of some metabolic product (or products) which is produced quantitatively in proportion to the work done by the heart. The amount of the chemical product produced for a given quantity of work is increased when the heart works inefficiently. Such inefficiency in cardiac work occurs especially when the diastolic blood pressure is elevated, because the heart has to exert more effort in raising the pressure of its contents above the diastolic aortic pressure

before it can expel the blood. This in part is also the cause for the inefficiency of the rapidly beating heart. A similar inefficiency occurs when the heart is failing, because the heart dilates in order to do its work.

The accumulation of the metabolic product which acts to stimulate pain is checked in part by a mechanical and in part by a chemical process. The first is a washing away of the substance by the circulating blood; the second is a local conversion to some other substance in the presence of oxygen. This pain producing substance will, therefore, increase in concentration whenever the circulation is slowed or whenever the oxygen content of the blood entering the coronary arteries is decreased.

Our work indicates that a pre-pain stage exists in which the metabolic product causing pain is increased in amount but not sufficiently to stimulate the pain end organs. As in the case of all sense organs, a certain threshold value must be reached before the end organs respond. In the pre-pain stage the concentration of the chemical product may vary within wide limits (from zero to the threshold value). This variability in concentration in the pre-pain stage is one of the reasons for our inability to predict whether or not a given set of circumstances will lead to a paroxysm of pain. It may explain in part why the factors required to cause pain are so variable in different patients and even in the same patient.

SUMMARY

In other words it would appear that the stimulus for pain is a metabolic product (or products) which can readily diffuse into the blood stream and which can be quickly altered in the presence of an adequate supply of oxygen. The accumulation of this product is dependent upon the amount and character of the physical work and the efficiency, on the one hand, and the quantity of the oxygen and blood supply on the other. When this substance reaches a concentration above the threshold of the pain end organs, pain results. This chemical product appears to be acid in character, or at least one that is additive with acid substances and is "neutralized" by alkaline substances. In all probability it is some substance like lactic acid or phosphoric acid formed during the catabolism of muscular activity.

Work remains yet to be done on many aspects of the problem of pain production, especially in accounting for the variations in pain responses under what seem to be similar conditions. An important factor responsible for this variability, it seems to us, is the inconsistency of the state of the pain receptors and pain pathways and the fluctuation in the sensorium for perception of pain sensation. Work on these phases is now in progress.

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PATHOLOGY OF CORONARY SCLEROSIS*

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COMPARATIVE study of a large series of coronary arteries from cases in which lesions of these vessels have been responsible for the fatal issue revealed histological differences which caused the cases to fall into two groups.† The first of these groups was found to include all of the younger members of the series with two exceptions. The second group included, with these exceptions, the older members of the series. The exceptions, on microscopical examination, were found to be secondary processes in coronary arteries in young men in which earlier thrombosis and repair had occurred, thus leading to conditions which produced lesions typical of the older group. The ages covered by the first group of fatal cases were from twenty-five to fifty-five years. The ages in the second group were from forty-seven years up to old age.

Microscopically the lesions of the first group were characterized by fibrosis and a minimal persistence of lipid cells. Per contra the lesions of the second group were distinguished by the massing of lipid cells and a relatively small amount of fibrosis. It became apparent that the differences in these two series were dependent upon a reaction to the presence of lipid cells in youth which caused a stimulation of connective tissue that tended to replace the lipid cells as they were deposited. In the older group this reaction was lacking and lipid cell deposits became so excessive, with attendant poor nourishment, that massive necrosis and formation of atheromatous cavities became the standard picture before death.

Since the differences described appeared to center about variations in the phenomena associated with the appearance of lipid cells in the lesions, resort was had to the study of the earliest lesions obtainable in an effort to determine the provenance of these lipid cells and the evolution of the lesions which were associated with them.

Three sources proved helpful: first, examination of the finer branches of the coronary arteries in young individuals whose main trunks had undergone advanced processes; second, the routine study of sections of

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†It has been the custom to lay open the coronary arteries with so-called coronary scissors. The use of scissors disturbs the normal relations and has tended to confuse the issue. Coronary arteries should be examined grossly by serial cross-sections with a sharp knife.

coronary arteries in young individuals who had died from any cause; third, the study of sections of the coronary arteries from cases of congenital heart disease.

It is recognized that the coronary arteries undergo at least more unusual and probably greater stresses than do other muscular arteries. The stresses are greater because the coronary arteries originate at a point where the highest arterial pressures are found, i.e., at the aortic ring.

Fig. 1.



Fig. 2.

Fig. 1.—Left coronary branch. Lipoid cells.

Fig. 2.—Left coronary branch. Note the normal internal "buffer" layer lining vessel apart from the atherosclerotic nodule, from same lesion shown in Fig. 1, at a lower level. Fat stained with sudan IV.

It is generally agreed by physiologists that those portions of the coronary arteries which lie in the subepicardial tissues are subjected during systole to pressure from the blood within the aorta and resistance from their myocardial branches which are being compressed by the contracting heart muscle, so that during a part of the cardiac cycle the pressures in the larger coronary vessels are unusual. It is further probable that the curve which the left coronary takes in its proximal inch, from an

orifice at right angles to the aortic wall to a position paralleling that wall, causes this portion of the vessel to undergo great stress. The origin of a large branch, the circumflex, probably also influences the pressures within this region, which is the favorite locus for serious or fatal forms of coronary atherosclerosis. The formation of a buffer layer of unstriated muscle and fibrous tissue in the subendothelial layer of the intima of the coronary arteries, and notably in the proximal portion of

Fig. 3.



Fig. 4.

Fig. 3.—Left coronary artery. Fibrosis near lumen—lipoid cells in depths.

Fig. 4.—Left coronary artery, from same lesion as Fig. 3. Fat stained with sudan IV.

the left coronary artery, as a standard finding in these vessels, even in early youth, is probably due to the great and unusual stresses which these vessels undergo.

The study of the left coronary artery in cases of congenital heart disease was fruitful, since unusual stresses were to be expected in the effort to overcome the developmental faults in the organ. The earliest atherosclerotic processes were found in the left coronary arteries of hearts with congenital disease.

Early stages in the progressive changes in the coronary artery of a young individual are well shown in the case of M. R., from whose left coronary the sections illustrated in Figs. 1 to 4 were obtained. A boy, eighteen years old at the time of his death, had a traumatized hip when seven years of age, followed by tubercular disease. He was treated through the following years but healing was accompanied by fixation of the hip joint. One year before his death he developed pleuritis with effusion, which subsided. Following a plastic operation to relieve the deformity of the hip, wound infection leading to streptococcus septicemia caused his death. The heart was submitted for routine coronary examination through the courtesy of Dr. Frederic Parker, Jr., by Dr. Edward Hayes. In Fig. 1 is seen the earliest lesion, a collection of lipoid cells beneath the intima of a branch of the left coronary artery. Fig. 2 is from a frozen section at almost the same location and is stained with sudan IV. The largest masses of the lipoids occur beneath the surface endothelium where they lie in large macrophages which are of recent origin. The lipoid cells which have migrated more deeply are smaller, and therefore the lipoid masses are smaller in the depths. Fig. 3 is from a section of the main left coronary artery above the orifice of the circumflex branch, which came off at a low level. The more advanced intimal process is marked by fibrosis of the inner layer, and spaces appear in the deep layer representing lipoid cells which had migrated more deeply as fibrosis progressed internally. A frozen section from the same location (Fig. 4), stained with sudan IV, reveals the lipoids now placed deeply beneath the inner fibrous layer, including some invasion of the media.

Beginning with these early lesions and proceeding through older processes to the late fatal lesions one can reconstruct the stages in the development of a disease, the beginnings of which may be found in the earliest days of life.

The earliest phenomenon is the deposit of free lipoid beneath the endothelium of arteries, i.e., lipoidosis. That stresses favor this deposit is suggested from the sites in which lipoid material occurs in the aorta, in which vessel they are most readily seen and have been most extensively studied. The deposit is evidently bland and does not provoke a fibrous reaction even in the very young.

The next step is the appearance of phagocytic cells which engulf the lipoid. The origin of these cells is still undetermined. They are not histiocytes, i.e., wandering connective tissue cells which have been resting in the tissue interstices. When these cells engulf and remove blood from a clot, for example, they can be seen throughout the tissues in the neighborhood of the clot. Nothing resembling this picture is seen in either human or experimental atherosclerosis. The cells may be monocytes which invade the regions where lipoid is being deposited or perhaps in some cases carry the lipoid into the regions where they come to rest.

Study of both experimental and human lesions makes me lean toward a belief that these cells arise locally from the subendothelial connective tissue.

The occurrence of lipid cells is progressive in most cases, new cells replacing the old in the surface layer as the old migrate to a deeper position or are replaced by fibrous tissue. In some cases they apparently

Fig. 5.

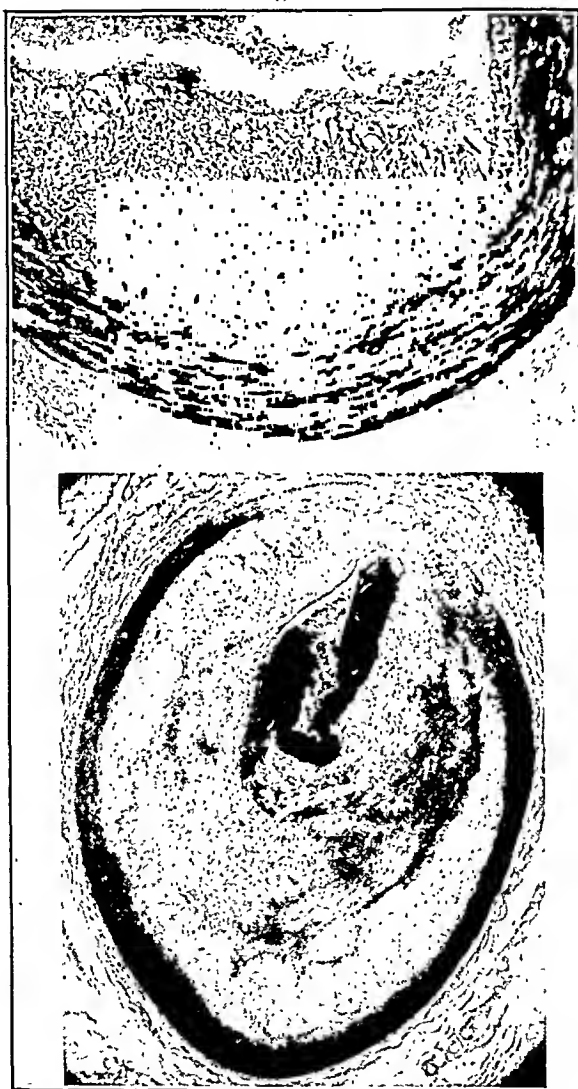


Fig. 6.

Fig. 5.—Early diffuse fibrosis developing in an early lesion of a small left coronary branch in a man of twenty-eight years, whose death was due to thrombosis of the left coronary artery, descending branch, beginning 1.5 cm. from orifice.

Fig. 6.—Typical fibrotic lesion with thrombosis in the descending branch of the left coronary artery of a man twenty-six years of age—eccentric fibrosis, nutritional necrosis of the layer farthest away from the lumen; acute fibrinous necrosis, terminal, near lumen. Note hypertrophy of media.

arise cyclically as indicated by the deposit of lipid cells and fibrous connective tissue in layers. The presence of lipid cells in the intima of the young, rabbit or man, is followed by a growth of fibrous tissue.

There is a suggestion that metabolism of the lipoids within the cells is responsible for the stimulating effect upon the neighboring connective tissue. Free lipid, in lipoidosis, does not have this effect. Fibrosis may be a focal process arising in the depths of the subendothelial tissue and progressively replacing the lipid cells, abolishing them as it spreads. More frequently it is a diffuse process, the reticular strands between the lipid cells increasing in thickness in the young as the cells decrease in size until finally the cells disappear (Fig. 5).

The nutrition of the newly formed fibrous tissue is dependent upon imbibition from the lumen. As the fibrotic layer increases in thickness, the nutrition of those portions which are most distant from the lumen tends to suffer. The lesions are usually eccentric, the narrowed lumen dislocated to one side (Fig. 6). In advanced lesions it is usual to find a crescentic region of necrosis of those portions of the intimal tissue most distant from the lumen, i.e., next to the media. The necrosis of the intimal tissue tends to be preceded or accompanied by a deposit of fat either in droplets or more diffusely along the broad collagen bands which often make up the deeper layers. This secondary fat deposit is probably related to degenerative changes in the fibrous tissue preceding necrosis. Lymphoid cell infiltration, absent from the early stages, tends to occur at this time.

The fatal issue most frequently arises as the result of a new and different type of necrosis, fibrinous or fibrinoid, arising focally in the fibrous tissue near the lumen and extending to the endothelial layer. Endothelial necrosis is followed by thrombosis. Or death may be due to inadequacy of the circulation through the narrowed lumen under conditions of stress without thrombosis. The more significant strains on the cardiac functions which tend to lead to fatal terminations are, in the order of their importance, indigestion, physical or psychic stress, and exposure to cold.

So much for the picture in youth. In older human beings the same appearance of lipid cells provokes no fibrosis. As new cells arise the older cells migrate or are forced to a deeper position, and ultimately large collections of these cells are found. Their nutrition is hazardous, depending as it does on imbibition, either from the lumen or sometimes from vasa vasorum. There is no true vascularization of the cell masses. The cells occur in spaces in a delicate linear reticulum either singly or in small groups in each space. Necrosis, usually massive, is the standard outcome. The lipoids are freed from the cells. According to the studies of Kimmelstiel¹ the lipid esters making up the contents of these atheromatous foci are mixtures of esters of cholesterol, phosphatides and cerebrosides. Cholesterol is a relatively insoluble hydrophobic colloid. Mixtures of its esters with those of other lipoids, which tend to form hydrophilic emulsions, increase the solubility of the cholesterol. When extensive necrosis of lipid cells occurs, the more soluble lipoids appear

to be largely absorbed from the mixture, leaving the relatively insoluble cholesterol, which crystallizes out. An atheromatous cavity may contain, therefore, some living lipid cells, cell detritus and crystals of cholesterol, together with fluid which may include lipid esters or free lipid.

The formation of an atheromatous cyst, cavity or "abscess," as it used to be called, presents a new hazard. Located in the intima of a muscular artery which is constantly undergoing dilatation and contraction is a cavity filled with semifluid material. Rupture of an atheromatous abscess in the aorta is attended with no considerable danger. The contents are broken up in the rapidly moving stream and the fine solid fragments diffused widely. In the coronary artery, rupture usually leads to obstruction of the lumen of the vessel near the point of rupture (Fig. 7) or to complete plugging of branches. The material is not broken up, but acts as a semisolid mass. In most cases death is sudden, but time

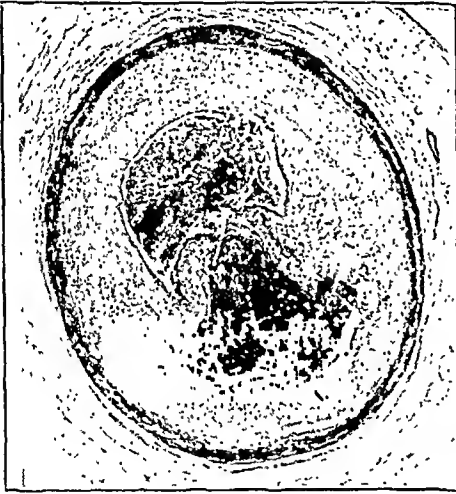


Fig. 7.



Fig. 8.

Fig. 7.—Point of rupture of atheromatous "abscess" in a man sixty-six years of age. Descending branch of left coronary artery 2 cm. from orifice. Lumen to the left and above filled with contents of "abscess." The vessel below this level contained clot and "abscess" contents.

Fig. 8.—Section of left coronary artery of a man sixty-two years of age. There are four atheromatous "abscesses." The central lumen is filled with clot and "abscess" contents. Probable rupture of the atheromatous focus nearest lumen.

enough has usually elapsed before the death to permit of clotting, either platelet or mixed clots arising (Fig. 8). As in the young, death may occur from coronary insufficiency, under stress, without rupture of an atheromatous cavity or thrombosis.

Mucoid changes in the later stages of atherosclerotic processes are not uncommon. They have the character of secondary degenerative processes and are met with usually in the intima but also in the media. In my experience so-called mucoid degenerated tissue is the substratum left in celloidin or paraffin sections after extracting lipoids by the fat solvents used in preparing tissue for paraffin or celloidin imbedding. In frozen

sections the lesions show free lipoids in the loci found in paraffin sections which exhibit mucoid changes.

Jenner's famous letter to Parry reporting calcification of the coronary arteries in the first case described in England, shortly following Heberden's coinage of the term "angina pectoris," has led most clinicians to look upon calcification of the coronary arteries as common and important. Calcification of the coronary arteries is a much later manifestation and less common than is calcification in the aorta. The deposit of lime salts in tissues is always an end-result, of monumental character, marking the site formerly occupied by living tissue. From any standpoint calcification is of no importance in the etiology of the lesions and is only significant in that a coronary vessel converted into a rigid tube is no longer subject to the influence of spasm of the media, though on the other hand it is no longer capable of dilating.

COMMENT

The lesions of atherosclerosis have been found in this series as early as the third day of life in the left coronary artery of a case of congenital heart disease (pulmonary and tricuspid atresia, cor triloculare). The lesions are not rare in coronaries of the first decade of life and are more common in the second decade. Fatal coronary thrombosis is found in the third decade and is relatively common in the decades which follow.

One can conclude therefore that atherosclerosis is a disease and not the inevitable consequence of age.

Study of the early lesions of atherosclerosis demonstrates that inflammatory elements are lacking. The lymphoid cell infiltration met with in the late stages is usually associated with secondary necrosis arising in the thickened intima, or appears in connection with terminal infections. The disease is therefore not inflammatory in origin.

The distinctions between the lesions of youth and old age are dependent upon a reacting ability in youth which results in fibrosis and upon a lack of this reaction in age.

Early lesions are always intimal with secondary effects on the other layers of the vessel wall. Though stresses are probably causative factors, morphological evidence of damage to the elastica is usually a secondary phenomenon. The media is more often hypertrophied, either locally or generally, than not. Evidence of other pathological change in the media is also secondary.

The lesions of atherosclerosis center about the deposit of lipid cells in the intima. One can conclude that this disease with its intimate relation to lipid cells is probably metabolic and results from the failure of a metabolism having to do with lipoids. Is there such a metabolism? Cholesterol is a lipid which is found in nature only in animal bodies

and their products. We think of it in terms of blood and bile cholesterol. We forget that cholesterol is the basic substance of every animal cell. Starling looks upon it as the stable material of the animal cell, relatively insoluble and fixed, serving as the framework, so to speak, of the cell, in the interstices of which the more labile substances undergo their metabolism. All of the human supply of cholesterol is derived from ingestion. None is synthesized, as far as is known. The herbivora synthesize cholesterol, possibly from the closely allied phytosterols, which have the same formula as cholesterol, but a different molecular arrangement. The cell needs for cholesterol are greatest in times of rapid cell division. Egg yolk rich in cholesterol is intended for the embryo. Milk, the fats of which contain cholesterol, is intended for the infant. The increase in blood cholesterol in pregnancy is a mobilization of this substance for the needs of the fetus in utero.

Man is the only animal that ingests eggs and milk throughout its lifetime. Man is also the only animal, as far as is known, that dies in early life of coronary sclerosis, and suffers almost universally from atherosclerosis in the later years of life.

Finally it is possible to reproduce the lesions of human atherosclerosis in the rabbit, by the feeding of cholesterol. Moreover human dietary experience in diabetic individuals supports the results of rabbit experimentation. Under excessively fat diets rich in cholesterol, atherosclerosis increased at such a rate as to focus attention, xanthomas were common, and atherosclerotic calcification of the leg arteries of children could be demonstrated by roentgen examination. Recent reports from the Joslin clinic indicate that under a lowered fat diet atherosclerosis is less outstanding, xanthomas no longer occur, and evidence of calcification of leg arteries in children is lacking.

Atherosclerosis has close analogies with that other important metabolic disease, diabetes. In both rabbits and man variations in idiosyncrasy to cholesterol are evident. As in diabetes the inheritance of a poor cholesterol metabolism may result in early manifestation of disease in the form of coronary sclerosis. As in diabetes the loss of efficiency of the metabolic machinery with age results in more frequent late manifestations of the disease. As in diabetes the secretion of a ductless gland appears to control the metabolism. Thyroid feeding is apparently capable of preventing the production of experimental atherosclerosis in the rabbit.

It has been observed for many years that arteriosclerosis was related to the inheritance of a familial diathesis or disposition which might manifest itself in the form of diabetes, gout, or obesity. As one glances at the group it is apparent that these are all disturbances of metabolism. The demonstration that atherosclerosis, the most important form of arteriosclerosis, is a metabolic disease, fits it appropriately into this group.

SUMMARY

From this study of the lesions of coronary sclerosis it is evident that the pathology of the disease as described in most textbooks needs to be rewritten. The descriptions of the pathology in these works have been based on cases of coronary sclerosis in which the patients have been hospitalized and in which secondary changes, including infarction with associated inflammatory reactions, have tended to obscure the picture. The material for this investigation has come from early lesions or from patients who have literally "dropped dead." This has permitted of the study of the primary process uncomplicated by secondary reactions.

These studies demonstrate that the standard lesion in coronary sclerosis is atherosclerosis; that the lesions arise from the entrance of lipoids into the subendothelial layer of the intima and their phagocytosis by cells referred to herein as lipid cells. In the young the presence of these lipid cells stimulates growth of fibrous tissue. As a result, the standard picture in coronary disease in the young is fibrosis, narrowing the lumen of the artery. Death is usually due to thrombosis. In the old the presence of lipid cells does not stimulate fibrosis. The cells accumulate in large masses, the nutrition of which becomes inadequate. Necrosis and autolysis result in liquefaction of the cell masses, and atheromatous "abscesses" result. Death is usually due to the rupture of an atheromatous "abscess" into the lumen.

It is possible to reproduce the lesions of coronary sclerosis in experimental animals by feeding the lipid, cholesterol, which makes up most of the lipid contents of atherosclerotic lesions.² The lesions, natural and experimental, are primarily intimal and lipid. Lesions of the elastica and media are secondary. Inflammatory reactions are late phenomena following necrosis and are not an essential part of the picture.

Atherosclerosis is a disease due to disturbances in the cholesterol metabolism and belongs with the other metabolic diseases, diabetes (carbohydrates), gout (purines), and obesity (fats).

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CORONARY SPASM AS A POSSIBLE FACTOR IN PRODUCING SUDDEN DEATH*

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INTRODUCTION

IN MEDICAL observations it is not always possible to get direct evidence for the solution of a problem. We then have to proceed by inference.”¹

Though many theories have been advanced to account for the pain in angina pectoris, the medical world in general has come to accept Mackenzie's thesis that the pain is of cardiac muscle origin, and is due to an inadequate supply of blood, leading to muscular exhaustion. The pain may be produced by overwork even when the blood supply is normal. It usually comes on during stress conditions, but also may come on hours after the effort which led to a muscle strain approaching exhaustion. In any case it depends upon the blood supply to the organ. A normal supply may be inadequate under conditions of great stress. A diminished supply may be inadequate under conditions of minor stress. The degree of pain which the individual suffers will depend upon the degree of inadequacy of the blood supply under the conditions obtaining, and upon the sensibility of his nervous system.

Attacks of what Mackenzie calls secondary angina pectoris may arise in individuals with a widespread hypersensitiveness of the nervous system. The attacks of angina in this group subside following removal of the cause of the nervous hypersensitiveness. As Mackenzie indicates, the primary cause is not cardiac, therefore the angina is secondary in character. This concept almost requires the deduction that under hypersensitive reflex excitability the blood supply to the heart muscle, in order to produce the pain, becomes inadequate during the attacks. The only reasonable manner of causing this inadequacy is by contraction of the coronary arteries under nervous control, thus limiting the blood supply. That the blood supply is adequate between the attacks is evidence that the quality of the blood is not the important factor, and that the heart muscle is not in a permanently exhausted state. The disappearance of all symptoms following cure of the local condition, in some other part of the body, which was responsible for the widespread hypersensitiveness of the nervous system, can be accepted as fairly good evidence that

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the cardiac circulation was unimpaired following the period of anginal attacks. All of this points to coronary artery spasm as the source of the attacks.

THE CONDITION OF THE MEDIA IN CORONARY ATHEROSCLEROSIS

Atherosclerosis of the coronary arteries is a primary intimal process in which the media may remain almost intact even in moderately advanced cases. Invasion of the media by lipoids or lipoid cells or by extension of the fibrous tissue from the intimal lesion is a secondary phenomenon. The media may indeed show general or focal hypertrophy. Atrophy, apart from that arising from extension of the intimal lesion, is not general or striking, except as a late phenomenon. The possibility

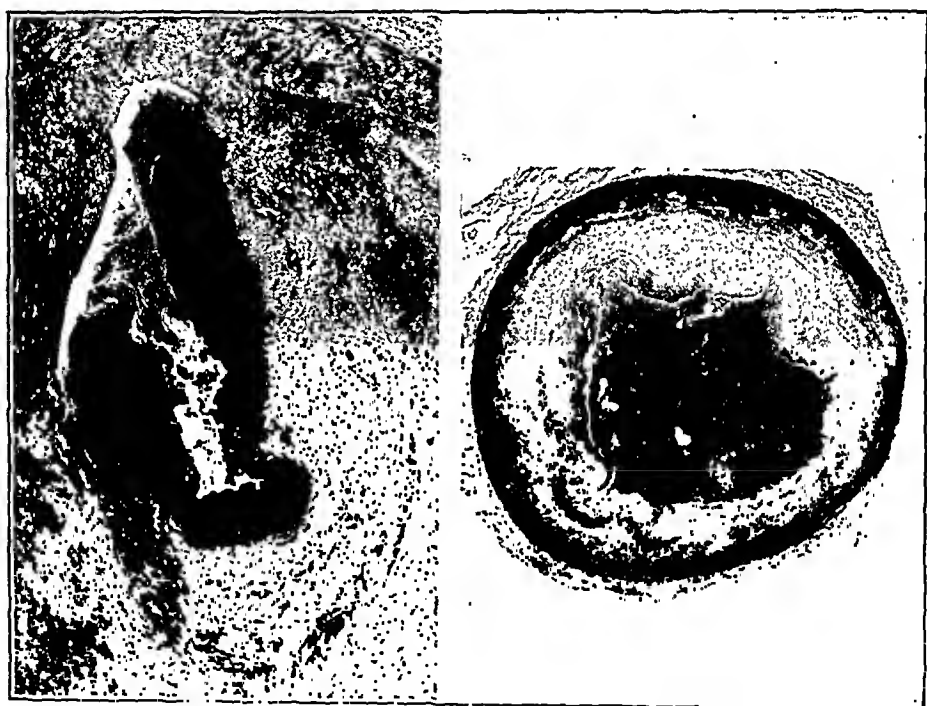


Fig. 1.

Fig. 2.

Fig. 1.—Coronary artery. H. W. T., male, twenty-six years old. Lumen with thrombus. Fibrinous subendothelial necrosis arising below lumen and extending to the endothelium on the left.

Fig. 2.—Coronary artery with thrombus. J. J. K., male, thirty-seven years old. Note angulation of lumen and hypertrophy of media.

that muscular spasm may exert a compressing force on the intimal lesion is therefore existent in most coronary vessels, excepting perhaps in advanced old lesions in which tubelike deposits of lime salts have made the walls rigid.

That spasm may be a factor leading to the fatal issue is suggested by:

I. MORPHOLOGICAL EVIDENCE

a. *Coronary Thrombosis.* In about 75 per cent of the cases showing fibrosis with narrowing of the coronary lumen, occurring in the young, there is found an acute type of fibrinous or fibrinoid necrosis appearing

in the subendothelial connective tissue and extending to the endothelium (Fig. 1). This type of necrosis, arising near the lumen, and therefore in well-nourished tissue, is in contrast to the slower nutritional type of necrosis arising in those portions of the intimal fibrous tissue most remote from the lumen, i.e., near the media.

The constant natural traumatism to which the endothelium lining vessels in the hands, feet, buttocks, and back must be subjected without harmful result indicate a high resistance of this tissue to violence. The indignities to which this layer may be subjected without damage in connection with certain operative procedures in which tissues are temporarily clamped tend also to establish the hardness of this layer. On the other hand, the foreign fibrous tissue which is formed in the sub-



Fig. 3.

Fig. 4.

Fig. 3.—Coronary artery. J. K., male, sixty-six years old. Atheromatous "abscesses" on either side of lumen. Atheromatous material in lower part of lumen. Thrombus with atheromatous material above.

Fig. 4.—Coronary artery. N. P., male, sixty-six years old. Rupture of atheromatous "abscess" below into narrowed lumen above. Note wide tearing of tissues.

endothelial layer of the intima in atherosclerosis is less well nourished and might well be injured by spasm of the media, while the endothelium lining the vessel is unharmed. Even though the endothelium is damaged, it is still able to function until some more efficient destructive agency comes into action. Extension of necrosis from the subendothelial tissues to the endothelium may supply this more efficient agency. Endothelial necrosis leads to thrombosis.

The angulation of the lumen found not rarely in the coronary arteries of young persons with fibrotic intimal thickening suggests an increased muscle tonus, notably when the media is hypertrophied. This picture depends in part upon connective tissue rigidity and redundancy when the vessel is contracted, but the contracting force is the muscle (Fig. 2).

b. *Coronary Obstruction by Rupture of Atheromatous "Abscess" Contents.* Rupture of an atheromatous cavity into the lumen or the rare reverse process, rupture from the lumen into the cavity, is the standard terminal lesion in older persons. It is possible that thinning of the membranous partition, which comes to be the only barrier between the cavity and the lumen, may lead by its own weakness to rupture, placed as it is in a muscular vessel. If this were true in general, the lesion should be marked by the filling of the cavity with blood, during systole, washing out the contents. Ordinarily the cavity is found more or less empty, indicating delivery of its contents by positive pressure. That rupture is not an artefact produced by the handling of the vessel post mortem is



Fig. 5.—Coronary artery. G. H., male, thirty-eight years old. Note hypertrophy of media. The pale foci extending into media below were occupied by lipoid. Section from point of greatest narrowing.

evidenced by the diffusion of atheromatous material through thrombi. Atheromatous material is not readily mixed with blood, notably clotted blood (Fig. 3).

The character of the tear in the limiting membrane and the endothelial lining of the vessel tends in many cases to negative the hypothesis of more or less passive rupture. Oftentimes the rupture is associated with splitting of the separating layer, not a mere tearing through. It is true that in some cases necrosis at the site of rupture has preceded the breach in the wall, but this is exceptional. Compression of the cavity contents and their forceful delivery through the rent in the wall best account for the appearances found (Fig. 4).

c. *Coronary Insufficiency*—with spasm? The following case is typical of a condition which suggests the possible influence of spasm.

G. H., an Armenian, thirty-eight years of age, 5 feet 6½ inches in height, body weight 156 pounds but with very fat abdomen, had always been in good health. His wife stated that he had never consulted a doctor, and had not suffered from indigestion. On the day of his death he accompanied his son, twelve years old, to a conservatory of music. The boy had been taking lessons on the violin, and the father was for the first time to be present during his son's lesson. Furthermore the teacher would play a duet with the boy. The father was much stirred emotionally in expectation of an experience to which he had looked forward. He collapsed in the office of the conservatory, was brought to a hospital, and pronounced dead on arrival. The indications were that death had occurred almost immediately after his collapse. The heart weighed 350 grams, with some left ventricular hypertrophy. The valves and cavities were normal. There were yellow opaque patches in the aortic arch about the ring, with slight narrowing of the orifice of the left coronary artery. The walls of the coronary arteries were thickened, for the most part moderately. Gross section of the left coronary disclosed longitudinal ridges in the inner layer, suggesting wrinkling of the thickened intima. There was no thrombosis. Microscopical examination of the left coronary artery revealed fibrosis of the inner layer of the thickened intima, abundant lipoid cells more deeply placed and focal lipoidosis of the media. The lipoid in these medial deposits merely mechanically separated the muscle fibers, without evidence of any reaction. The media was definitely hypertrophied (Fig. 5).

The narrowing of the lumen of the vessels by the atherosclerotic intimal lesions was not adequate, of and by itself, to account for the death. The peculiar longitudinal folding of the thickened intima suggested an increased tonus of the hypertrophied muscle layer consistent with a concept that coronary spasm had been a factor in producing the sudden death.

II. ANGINAL ATTACKS FOLLOWED BY SUDDEN DEATH

a. *With Normal Coronary Arteries.*

V. I., a Lithuanian, twenty-three years of age, was an agent in a gambling number game. His father had dropped dead when forty-five years old. The son had had attacks of chest pain lasting several minutes during which he "could not lift" his left arm. The last attack occurred one month prior to his death. March 8, 1934, he had been drinking, came in to meet his employers, and was excoriated verbally and told to go home. He entered a bus, collapsed in the bus, could not be roused, and was removed in an emergency ambulance to a hospital where he was pronounced dead. Post-mortem examination revealed a heart weighing 340 grams, with slight left ventricular hypertrophy. The valves and cavities were normal. The coronary arteries were grossly normal throughout. The arch of the aorta was thin with a few pinhead yellow opaque foci. The aorta was thin, smooth, and elastic, with delicate yellow streaks along the line of intercostal orifices and about the orifices of abdominal branches. The pia-arachnoid was moderately injected and contained a moderate amount of clear serous fluid. The stomach contents, 400 c.c. of a yellow paste, had a strong odor of beer.

Microscopically the coronary arteries were lined by a "buffer" layer of unstriped muscle and fibrous connective tissue (Fig. 6), perhaps somewhat thicker than normal (Fig. 7). There was no evidence of atherosclerosis at any point.

No adequate cause of death was found at post-mortem examination in this case. The degree of alcoholism was not great enough to kill, and was particularly not adequate to kill suddenly. Chemical examination of

the stomach contents revealed no evidence of a poisonous agent. The history of a father who dropped dead, the personal history of attacks which were anginal in character, and the suddenness of the death following a scolding with threats of discharge, suggest that coronary spasm may well have been the cause of the attacks, and that the terminal one led to the death.

b. *With Minute Atherosclerotic Lesions.*

B. E. L., male, forty years of age, single. This man was an overseas veteran who had suffered attacks of angina over a period of years. He claimed that these were a sequence of his war exposure. The Veterans Bureau discredited his claims on the ground that he was a malingerer. He had had an attack of distress in the chest two weeks before his death. He did not sleep well on the night before his death because of discomfort in his chest and did not go to work in the morning. He went out at 9 A.M., returned in twenty minutes. At 11 A.M. he again had acute

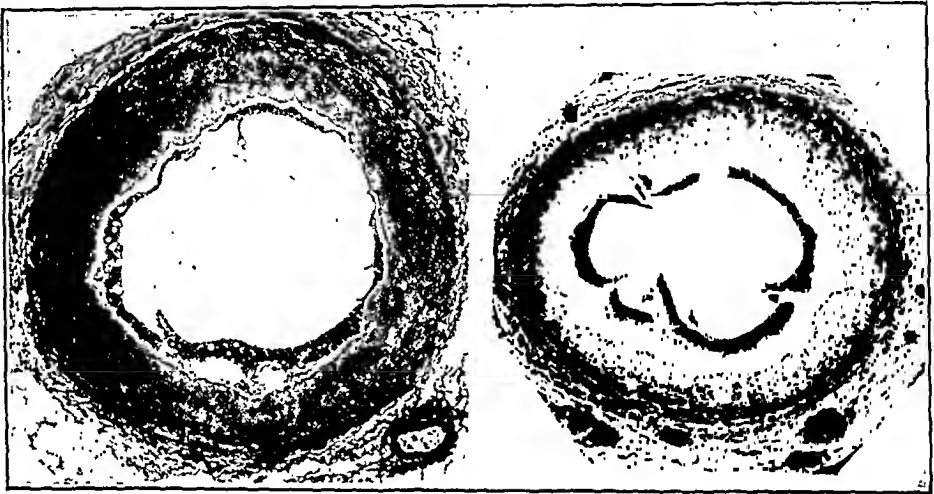


Fig. 6.

Fig. 7.

Fig. 6.—Coronary artery. V. L., male, twenty-three years old. Somewhat thickened "buffer" layer lining vessel. Hypertrophy of media.

Fig. 7.—Coronary artery. M. R., male, fourteen years old. Normal coronary with "buffer" layer, somewhat thicker than average but within normal limits—for comparison with Fig. 6.

pain in the upper chest. A physician was called, who found him undergoing an attack of angina. He had drunk some peppermint, and was given $\frac{1}{4}$ gr. morphine in tablet form. Shortly afterward he was heard breathing heavily, had vomited and died suddenly at 1:30 P.M. Post-mortem examination disclosed a heart of normal size, the valves and cavities of which were normal. The muscle was homogeneous. The aorta was thin, smooth, and elastic. In the coronary arteries were found rare minute yellow foci, but the lumina were free, though vessels were of small caliber. The other organs were normal save for mild edema of the brain.

Death in this case demonstrated that the man was not a malingerer. A malingerer may appear to put one foot in the grave, but is careful to remove it before dangerous consequences arise. Again, in this case no adequate cause of death was found. The anginal attack seen by the physician preceding the death was of typical character and the presumption is that the previous attacks in which he was unattended

medically were similar. The amount of atherosclerosis of the coronary arteries was so slight that it might have been overlooked except for a thorough search.

COMMENT

The clinical and pathological material here presented can be, of course, only suggestive as to the possible rôle of coronary spasm in leading to attacks of angina or in producing sudden death. Frequently one sees cases of sudden death, particularly in hypertensive heart disease, in which post-mortem examination discloses coronary sclerosis without thrombosis, and with lumina of the coronary arteries large enough apparently to supply the needs of the heart muscle. The acute anginal attack or the death has occurred under physical or psychic stress, or accompanying indigestion or exposure to cold, or following these experiences. In many cases death occurs during the night while the patient is asleep. Asphyxiation by position while lying on the face or with the head buried in a pillow is met with almost wholly in epileptic or alcoholic persons. Other human beings who lie in dangerous positions escape asphyxiation by being awakened, the awakening usually coming following a nightmare. After such an awakening the individual comes to with a feeling of relief, as though he had been through a stressful experience. It is my belief that coronary deaths during sleep may be associated with the stresses which accompany nightmares.

One can understand how an acute need for blood under stress in hearts with rigid narrowed coronary lumina, due to calcification, could lead to anoxemia of the heart muscle and a resulting fatal issue. When the lumen is adequate and unobstructed in a still elastic vessel, the possibility that narrowing of the lumen by spasm under stress is responsible for the anoxemia presents the most reasonable explanation of the phenomena observed.

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INVERSION OF THE T-WAVE IN LEAD I OR II OF THE ELECTROCARDIOGRAM IN YOUNG INDIVIDUALS WITH NEUROCIRCULATORY ASTHENIA, WITH THYROTOXICOSIS, IN RELATION TO CERTAIN INFECTIONS, AND FOLLOWING PAROXYSMAL VENTRICULAR TACHYCARDIA*

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INTRODUCTION

IN THE course of routine electrocardiography our attention has been drawn occasionally to inversion of T in Leads I or II of the electrocardiogram in individuals who have shown no clear evidence otherwise of heart disease. Because inversion of T has been closely associated, and correctly, with serious myocardial disease, any exceptions deserve attention. Some of these exceptions are well known; some others, less commonly recognized, are herewith reviewed together with observations on neurocirculatory asthenia, a syndrome in which significant inversion of T has not been reported heretofore.

SELECTION OF CASES

Criteria designed rigidly to exclude patients in whom there existed some known causes for an inverted T, other than those under consideration, governed the choice of cases. Only patients in the younger age group were included. The history, physical examination, roentgenological and laboratory data were used to avoid instances of organic heart disease which are well known to cause inversion of T, namely, such affections as coronary disease, acute rheumatic infection, and acute or chronic pericarditis, and the inverted T associated with marked ventricular hypertrophy or intraventricular block. None of these patients was taking drugs of the digitalis series; none was suffering from myxedema, chronic nephritis, or drug intoxication. Each patient was reexamined at least once, and most were examined repeatedly over a period of months or years.

For greater convenience the patients in this series have been appropriately grouped, and each group will be considered separately. The case histories appended make an extensive discussion of the symptomatology unnecessary.†

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†The case reports upon which this study is based will be published in the reprints of this article.

NEUROCIRCULATORY ASTHENIA

This group comprises 7 patients, 3 males and 4 females, with an average age of twenty-four and one-half years. In not a single case was organic disease of any description found on repeated examination. In one patient an additional diagnosis was made of probable paroxysmal tachycardia; there was a history of a single attack lasting for five minutes five months before our examination. In one other patient an additional diagnosis was made of an anomalous electrocardiogram, consisting of a short P-R interval and wide QRS wave as reported by Wolff, Parkinson and White¹ in normal young persons.

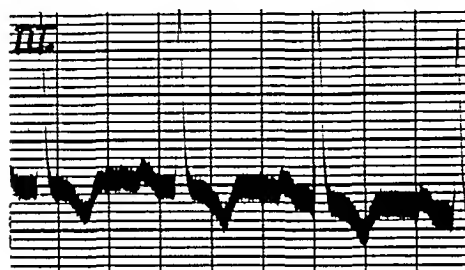
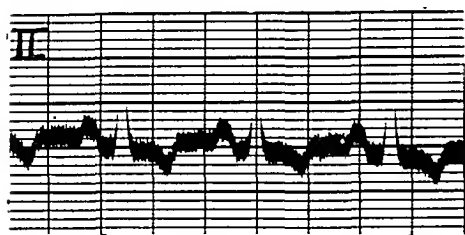
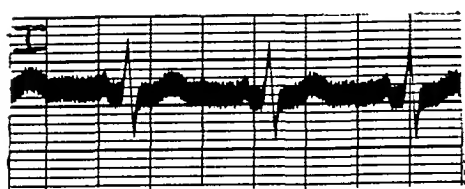
The chief subjective symptoms were similar in each patient and were induced by abnormally small effort. Of the 7 in this group, all complained of palpitation, 6 were easily fatigued, 5 complained of dyspnea, and 5 suffered pain or ache in the region of the heart. All but two complained of "nervousness"; dizziness, faintness, and excessive sweating were less common complaints.

The heart size, measured from orthodiagram or teleroentgenogram, was not abnormal in a single instance. Heart rates were uniformly rapid and averaged 112 (limits 95 and 130) in the initial electrocardiograms. In 4 patients no murmurs were heard; in 3 an inconsequential systolic murmur was detected. The blood pressures of all were normal, as were the Wassermann and basal metabolic rate determinations when these tests were carried out. Other routine or special laboratory tests revealed nothing abnormal. As all the patients were reexamined at a later date, the possibility of overlooking incipient disease was practically eliminated.

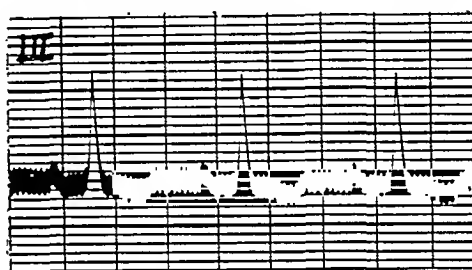
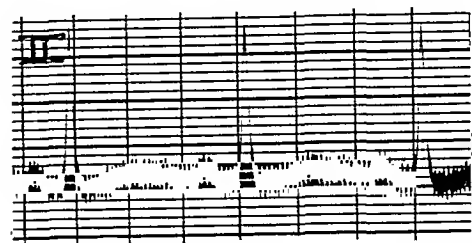
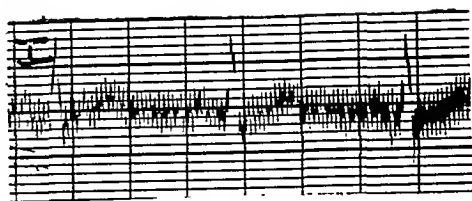
At the time of the initial examination the electrocardiogram in each instance showed an upright T in Lead I and an inverted T in Leads II and III. No other important electrocardiographic abnormalities were found.

At the time of the last examination one patient was entirely well; five showed improvement of greater or lesser degree; while one remained unchanged. None had developed organic disease of any system; the clinical heart findings were not significantly altered except for the slower heart rates. Final electrocardiograms showed an upright T in Leads I and II and inverted T in Lead III in each instance. This change to upright T in Lead II was not associated with significant changes in the P or QRS waves. The heart rates, measured from the electrocardiograms, varied from 75 to 100, and the average was now 88.

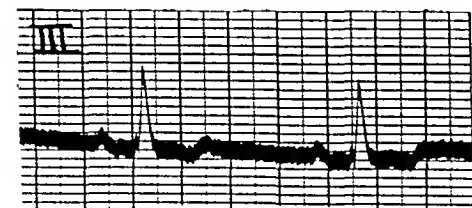
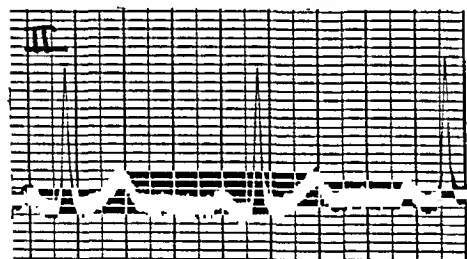
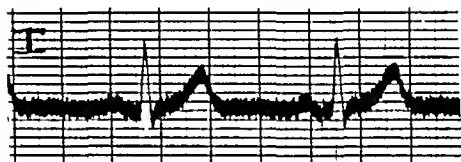
Comment.—We have no good explanation for the significant inversion of T in the electrocardiograms of these patients. It hardly seems likely that the unknown mechanism behind neurocirculatory asthenia alone is responsible because this association is rare. There was neither



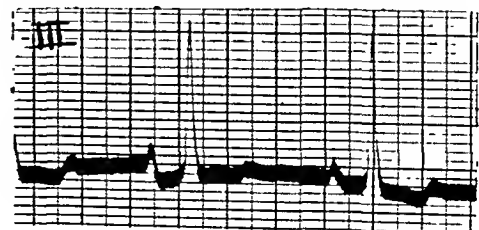
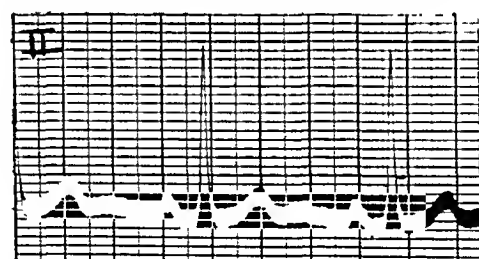
Jan. 20, 1930



May 23, 1930



Aug. 26, 1932



Jan. 9, 1934

Fig. 1.—Electrocardiograms from Case 1 (boy aged fourteen years; neurocirculatory asthenia). January 20, 1930; showing inversion of T in Leads II and III. May 23, 1930; T in Lead II now upright but rather low. August 26, 1932, and January 9, 1934; T in Lead II normal.

recognizable inadequacy of the coronary circulation nor any other factor known to cause inversion of T.

Although a very occasional finding, inversion of the T in neurocirculatory asthenia retains importance because of the serious diagnostic error to which it may lead. A number of similar cases, in which there was strong evidence that important organic disease did not exist, we have not included because of their greater age or because of their failure to return for reexamination.

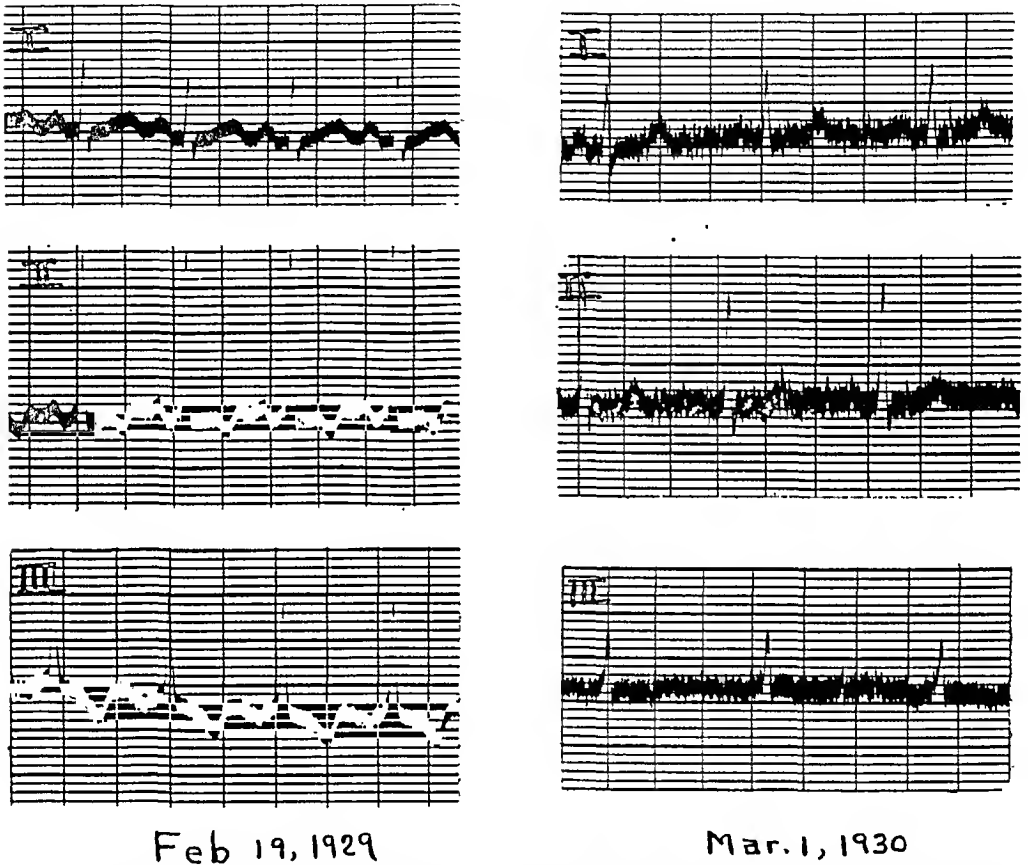


Fig. 2.—Electrocardiograms from Case 8 (girl aged twenty years; thyrotoxicosis). February 19, 1929, before thyroidectomy; showing inversion of T in Leads II and III. March 1, 1930, after thyroidectomy; showing upright T in Lead II and isoelectric T in Lead III.

THYROTOXICOSIS

This group comprises 4 patients, 1 male and 3 females, with an average age of twenty-four and one-half years. Each presented signs and symptoms characteristic of uncomplicated thyrotoxicosis. The heart was very slightly enlarged in two, and in one the systolic blood pressure was abnormally high—164 mm. mercury systolic and 50 mm. diastolic. Following subtotal thyroidectomy the heart size and blood pressure in these instances returned to normal. No other diagnosis was made in the case of any of these patients while under our care.

The initial electrocardiograms were taken shortly after entry into the hospital and before the administration of iodine, at which time

the average basal metabolic rate was plus 44. In three instances T was upright in Lead I, and inverted in Leads II and III. In one instance T was isoelectric in Lead I, and inverted in Leads II and III. The average heart rate, measured from the electrocardiograms, was 140. There were no other significant electrocardiographic abnormalities.

Following subtotal thyroidectomy each patient experienced relief from the distressing symptoms, and the basal metabolic rates returned to normal. Reexamination later revealed nothing abnormal, and the electrocardiograms showed upright T in Leads I and II in each instance.

Comment.—It is not generally agreed that T varies in form or direction in thyrotoxicosis. Hoffman² and others since have described the association of a high T-wave with this condition; whereas Lewis³ could find no definite alteration in the shape of the ventricular complex. White and Aub⁴ found only very limited parallelism between the basal metabolism and the amplitude of T in 27 patients with thyrotoxicosis. Willius⁵ and his coworkers reported inversion of T in 5 instances of thyrotoxicosis but believed coronary disease responsible. More recently, Pardee⁶ has written that "curves resembling the coronary T-wave may be seen [in hyperthyroidism]. When the toxicity passes off, the T-wave of these patients will return to normal."

In the cases we present, the evidence is presumptive that the thyrotoxicosis was responsible for the inverted T. Whether or not there was in these patients some degree of relative coronary insufficiency, not however causing angina pectoris but dependent on the thyrotoxicosis, we have no way of knowing. It is true that infrequently relatively young patients with thyrotoxicosis suffer from angina pectoris which disappears when the basal metabolic rate returns to normal.

INFECTION

This group comprises 5 patients, 1 male and 4 females, with an average age of twenty-five years. Each suffered from some infection (not rheumatic or diphtheritic) either shortly before or at the time of the initial examination. None had any cardiac complaint, and at no time was there clinical evidence of organic heart disease. No abnormality in size or shape of the heart was found. In two, slight inconsequential systolic murmurs were heard. The blood pressures of all were normal. In 3 of the 5 patients the initial electrocardiogram showing an inverted T was taken during the illness, while in the remaining two it was taken six weeks and four months, respectively, after the infection. T in Lead I was upright in all instances, T in Lead II was inverted in three and diphasic in two, and T in Lead III was inverted or diphasic in all. The average heart rate, measured from the electrocardiograms, was 115. There were no other significant electrocardiographic abnormalities. One patient died on the day the electrocardio-

gram was taken; the heart was judged normal at necropsy. Three of the remaining four became well; and electrocardiograms, taken two, two and one-half, and twelve months, respectively, after the infection, showed normal T-waves in Leads I and II and inverted T-waves in Lead III. The remaining patient (Case 12) at the time of re-examination had a mild recrudescence of her chronic bronchopulmonary infection, and the electrocardiogram showed sinus arrhythmia, rate 110, upright T in Lead I, slightly upright T in Lead II and inverted T in Lead III. Some details concerning the return from an inverted to an upright T can be gained from the case summaries.

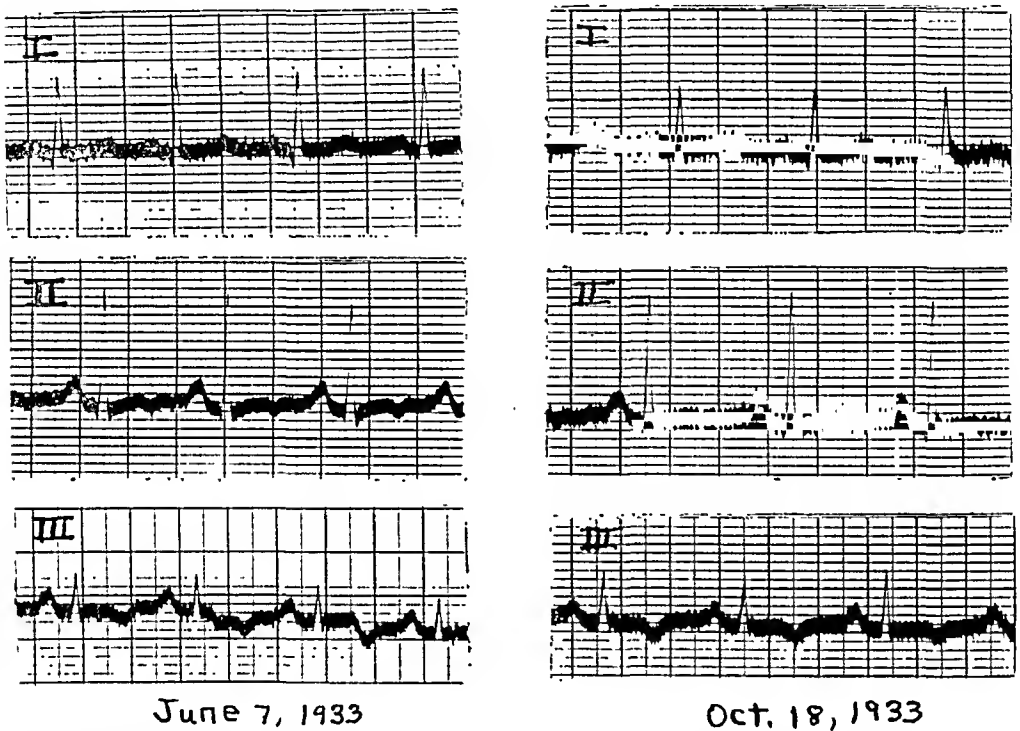
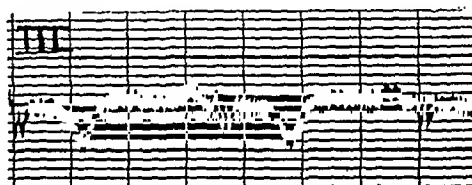
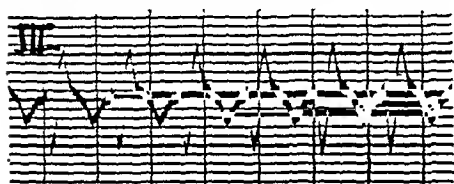
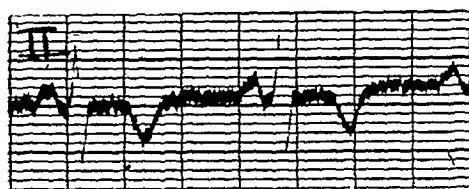
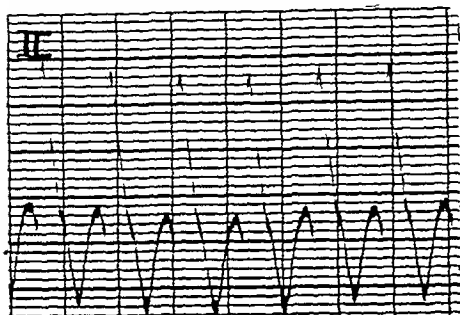
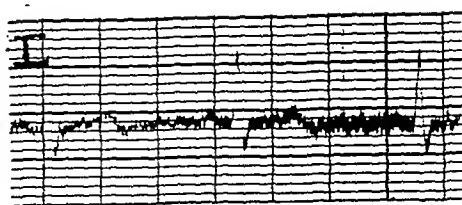
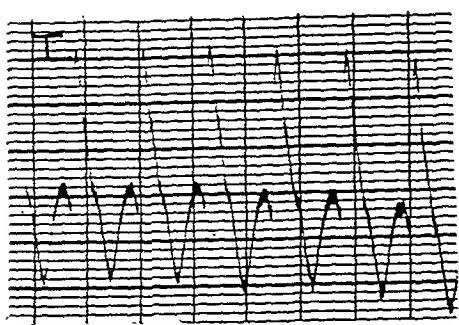


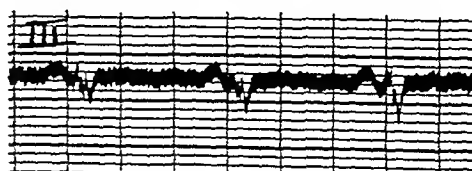
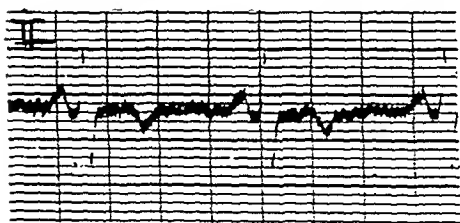
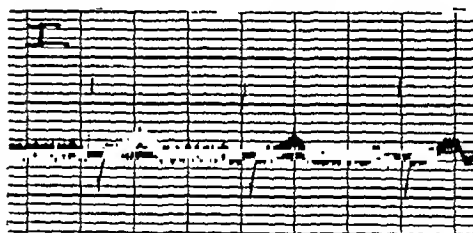
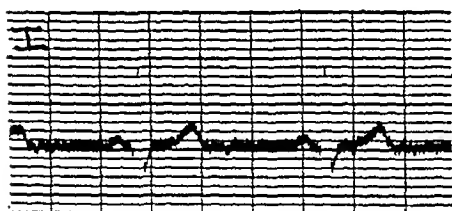
Fig. 3.—Electrocardiograms from Case 12 (woman aged twenty-seven years; chronic bronchopulmonary suppuration). June 7, 1933, during acute phase; showing inversion of T in Leads II and III. October 18, 1933, during mild recrudescence; showing slightly upright T in Lead II and inverted T in Lead III.

Comment.—Since the time of Kraus and Nicolai⁷ (1910) it has been known that the T-wave may be depressed by the action of heart poisons. The first observations illustrating the effect of infections in depressing the T-wave of the electrocardiogram of human beings were made by Smith,⁸ who published records showing inversion of T in Leads I and II following diphtheria. Later Cohn and Swift⁹ showed that inversion of T may occur in acute rheumatic fever. More recently inversion of T has been shown to occur in relation to various infections. This relationship of the heart to infections is sometimes declared by certain clinical signs or symptoms, but at other times the chief or sole discoverable sign is furnished by the electrocardiogram.



Nov. 21, 1928

Nov. 22 1928



Nov. 23, 1928

Jan 9, 1929

Fig. 4.—Electrocardiograms from Case 17 (man aged thirty-three years; paroxysmal ventricular tachycardia). November 21, 1928, showing the abnormal rhythm. November 22 and 23, 1928; normal rhythm with inversion of T in Leads II and III. January 9, 1929; T in Lead II is now upright and in Lead III isoelectric.

PAROXYSMAL VENTRICULAR TACHYCARDIA

This group comprises two young men in robust health. In both, the only evidence of cardiac disability was furnished by a single paroxysm of ventricular tachycardia lasting less than twenty-four hours. The onset of the paroxysm was not provoked by any unusual incident in either case; the offset occurred spontaneously in one and after 9 grains of quinidine sulphate in the other. In one the first electrocardiogram taken after the paroxysm showed normal rhythm at a rate of 52, inversion of T in Lead I, high T in Leads II and III, short P-R interval with widened QRS complexes,¹ and right axis deviation. In the other, the first electrocardiogram taken after the paroxysm showed normal rhythm at a rate of 80, upright T in Lead I and inverted T in Leads II and III. Both individuals were examined repeatedly over a period of two months and two years, respectively, and no physical abnormality was detected. Later electrocardiograms taken at intervals showed a gradual return of the abnormally inverted T-waves to the upright form.

Comment.—We believe the paroxysms of ventricular tachycardia to be in some way responsible for the temporary inversion of the T-waves. However, on looking over the tracings of all our other cases showing paroxysmal ventricular tachycardia or paroxysmal auricular tachycardia, flutter, or fibrillation, we were unable to find further examples.

MISCELLANEOUS

This group comprises five patients with an average age of twenty-six years. One had no disease of any nature; the diagnosis in the remainder was either complicated or not made. The case summaries may be referred to for details. The initial electrocardiograms all showed inversion of T in Leads II and III and an average heart rate of 119. At the time of our last examination the electrocardiogram in each case showed upright T in Leads I and II, and an average heart rate of 102.

Comment.—Each patient in this group presented a problem in diagnosis. With two exceptions, in whom infection (in one of them diphtheria one year before) may have played a rôle, an explanation for the inverted T-waves is not to be found in medical writings. It is thus evident that on rare occasions one finds inversion of T in Leads I and II without apparent cause.

FURTHER DISCUSSION

The T-wave is much less stable than the other electrocardiographic deflections. Although its mechanism is obscure, we are familiar with certain secondary factors that may change its form and direction.

Chief among these are alterations of coronary circulation, disturbances of nervous origin, the action of toxins or drugs, and change in position of the heart.

We are not unmindful that one sometimes finds extensive coronary sclerosis at post-mortem examination in young individuals who may or may not have had symptoms of coronary origin. However, in the cases herewith presented we were unable to determine that the coronary circulation was inadequate either as the result of the particular condition diagnosed or independent of it. We are not even justified in assuming a relative coronary insufficiency with the heart working under unfavorable conditions.

Human and animal observations agree in showing that T may alter through nerve stimulation or depression. The accelerated heart rate recorded in many cases in this series was not always adequately explained, and it is interesting that sometimes the change from inverted to upright T was associated with a fall in rate.

With the possible exception of those cases in which infection was present there was no evidence of toxic injury to the myocardium. Likewise there was no evidence of drug intoxication, or that change in position of the heart had occurred.

Thus we have found that inversion of T in Leads I or II is by no means invariably allied with causes commonly held to produce such inversion. We have selected instances in which neurocirculatory asthenia, thyrotoxicosis, infection, or paroxysmal ventricular tachycardia was the only associated finding. This association is presented without concluding that the above disorders are even secondarily responsible for T inversion. Of chief importance is the correct interpretation of the electrocardiographic findings which must still be done by correlation with the patient's history and physical examination. To emphasize the correctness of our interpretation we have included only patients in a young age group and those whom we have observed over a considerable period of time. It is not unreasonable to assume that some such patients are now wrongly thought to have serious organic heart disease. Many others in whom there was strong presumptive evidence that significant heart disease did not exist were not included in this series because of their greater age or their failure to return for reexamination.

The T-wave in Lead III was more inverted than the T-wave in Lead II in each instance recorded above, and remained inverted in most instances (16 out of 23) after the T-wave in Lead II had ceased to be inverted. It is well recognized by those dealing with routine electrocardiography that the inversion of T in Lead III is frequently found in normal individuals.

SUMMARY

1. We have presented 23 cases in which significant inversion of the T-wave of the electrocardiogram was not associated with the usual known causes for such inversion.

2. The reason for T inversion in these cases is unknown.

3. The importance of this finding is that it points to the need of caution in the diagnosis of serious heart disease when inversion of the T-wave in Lead II of the electrocardiogram is the only abnormal finding.

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ARTERIOLAR LESIONS OF SKELETAL MUSCLE IN HYPERTENSION*

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IT IS now well established that individuals dead of so-called essential hypertension usually show a more or less severe involvement of the smaller renal arteries—the arterioles. Similar lesions of the arterioles are often found in other organs, i.e., liver, spleen, pancreas, adrenals, intestines, nervous system, and retina, but opinions differ as to the occurrence of such lesions in somatic muscle. Most observers in the past, notably Jores, Fahr and, in this country, Bell and Fishberg, have reported that the voluntary muscles in hypertensive disease rarely show arteriolar lesions. Recently, however, Keith and his associates, using as their criterion the quantitative relationship between the thickness of the vessel wall and the diameter of the lumen, reported arteriolar lesions in voluntary muscle in certain types of hypertension.

In this work we have rated arterioles not according to deviation from Keith's normal ratio but according to the examiner's concept of what constituted a diseased vessel. All ratings were made by one of us (D.P.S.), and our criteria, so far as they can be expressed in units, are (1) thickening of the vessel wall, (2) hyalinization of vessel wall, (3) other pathological changes such as fatty, fibrous and necrotizing lesions, (4) size of lumen. A standard hematoxylin and eosin stain following formalin fixation was used throughout. In this work care was taken to rate only the smallest vessels. A case was rated according to the severest lesion observed, regardless of variation in the same section or in sections from different voluntary muscles in the same section. Our ratings were from one to four plus. We believe that a vessel rating three to four plus by our criteria would be regarded by most pathologists as a seriously diseased arteriole.

Sections of skeletal muscle were taken from 426 cases and the arterioles were rated objectively, with no knowledge on the part of the observer of the clinical diagnosis in the case. The patients varied in age from the first day of life to the ninth decade. Time will not permit a detailed discussion of this material, but one interesting fact appears established, namely that in 68 per cent of a series of 386

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autopsies there was a definite relation between the state of the arterioles in the kidney and those in the skeletal muscle.

Included in the above material was a series of cases of diffuse vascular disease with hypertension, carefully studied clinically. We include for discussion here only those patients dying under the age of forty-six years. This arbitrary age limit was set in order to eliminate the possible rôle of an age factor in arteriolar disease. The pertinent data in this series are shown in Tables I and II.

TABLE I

ARTERIOLES IN SKELETAL MUSCLES AND KIDNEY IN 24 AUTOPSIED CASES OF HYPERTENSION, PATIENTS UNDER FORTY-SIX YEARS OF AGE

NAME	AGE	SEX	RACE	MEAN BLOOD PRESSURE		ARTERIOLES		CAUSE OF DEATH	HEART WEIGHT GRAMS
				SYSTOLIC	DIASTOLIC	MUSCLE	KIDNEY		
C. G.	30	F	Black	220	140	3-4+	4+	Uremia	425
E. W.	33	F	Black	240	150	3-4+	3-4+*	Uremia	400
F. J.	33	F	Black	170	120	2-3+	2-3+	Cardiac	400
M. T.	35	F	Black	240	110	1+	3-4+*	Uremia	575
L. B.	35	F	Black	260	160	3-4+	4+*	Uremia	475
M. M.	38	F	Black	215	140	2+	3-4+*	Uremia	375
M. C.	39	F	Black	225	125	4+	3-4+	Cerebral hemorrhage	425
E. M.	40	F	Black	250	180	3-4+	3-4+	Pneumonia	375
M. G.	40	F	Black	230	125	2+	2-3+	Cardiac	700
M. D.	41	F	Black	210	125	3+	4+*	Uremia	625
R. R.	27	M	Black	190	130	4+	3-4+*	Uremia	650
L. W.	37	M	Black	210	150	3-4+	4+*	Uremia	†
C. H.	37	M	Black	240	160	1+	3-4+*	Cardiac	675
J. S.	39	M	Black	220	140	2-3+	4+*	Cardiac	650
J. L.	42	M	Black			2-3+	2-3+*	Uremia	650
W. J.	43	M	Black	210	145	2+	4+*	Pneumonia	500
O. D.	45	M	Black	240	150	3-4+	4+*	Uremia	570
H. T.	32	F	White	230	150	2-3+	3-4+	Cardiac	650
D. B.	33	F	White	230	130	3-4+	3-4+	Cardiac	600
C. N.	41	F	White	230	145	3-4+	3-4+*	Uremia	425
J. C.	44	F	White	220	120	3+	3+	Cerebral hemorrhage	400
P. H.	45	F	White	220	120	4+	4+	Uremia	450
E. K.	35	M	White	195	155	2-3+	4+	Cardiac	500
E. B.	37	M	White	220	130	2+	3+	Cerebral hemorrhage	500

*Necrotizing arteriolar lesions.

†Heart not obtained.

In Table I are the data on 24 necropsied cases in which the arteriolar lesion of skeletal muscle is compared with that of kidney. In Table II are data on 25 cases in which were were unable to secure a necropsy but in which a biopsy specimen of the pectoralis major muscle was studied. Of those individuals dying under observation in this series the cause of death is indicated.

Clinical aspects of the two groups may be considered as follows. *Age:* As mentioned above, all patients were under forty-six years of age. The youngest was sixteen years. The average age at death was 36.2 years. *Race:* Noteworthy is the preponderance of negroes. In

spite of the fact that our hospital population is less than 25 per cent colored, fatal hypertensive disease under forty-six years of age occurred about three times as often in the black as in the white race. *Sex:* There were 30 females and 19 males. The widely held view that vascular disease is more prevalent in males than in females is not confirmed by this series. Thirty, or 61 per cent, of the patients were females and 19, or 39 per cent, were males. Twenty females were black and 10 white; 17 males were black and only 2 were white. In both

TABLE II
ARTERIOLES IN SKELETAL MUSCLE (BIOPSY) IN 25 FATAL CASES OF HYPERTENSION,
PATIENTS UNDER FORTY-SIX YEARS

NAME	AGE	SEX	RACE	MEAN BLOOD PRESSURE		ARTE- RIOLES BIOPSY MUSCLE	CAUSE OF DEATH
				SYSTOLIC	DIASTOLIC		
A. C.	26	F	Black	175	130	2-3+	Uremia
G. C.	28	F	Black	200	135	3+	Cardiac
E. W.	28	F	Black	235	155	2-3+	
I. N.	29	F	Black	180	124	3-4+	
N. D.	37	F	Black	220	145	3-4+	
A. S.	38	F	Black	185	130	3-4+	Uremia
M. P.	39	F	Black	235	165	2-3+	
M. T.	39	F	Black	190	140	3+	
E. B.	40	F	Black	195	135	3+	Cardiac
C. D.	43	F	Black	235	165	3-4+	Cardiac
F. S.	23	M	Black	195	145	2-3+	
L. S.	30	M	Black	180	118	2+	Cardiac
B. F.	32	M	Black	170	135	3+	Uremia
E. S.	32	M	Black	220	170	2-3+	
E. M.	36	M	Black	190	120	1-2+	Uremia
W. W.	38	M	Black	260	135	2-3+	
S. W.	39	M	Black	180	120	3-4+	
C. S.	41	M	Black	195	118	4+	Cardiac
J. O.	42	M	Black	235	180	2-3+	
F. B.	45	M	Black	170	100	3+	Uremia
J. W.	16	F	White	212	155	2-3+	Cardiac
M. R.	32	F	White	220	145	2-3+	
T. C.	30	F	White	230	140	3-4+	
R. M.	43	F	White	215	135	4+	Uremia
M. C.	40	F	White	240	165	2+	

rates, therefore, in this series the females predominate. *Blood pressure:* The blood pressure readings represent the average of a number of determinations of the systolic and diastolic blood pressures during the period of clinical observation. In most instances the systolic pressure was above 200 mm. and the diastolic above 120 mm. of mercury, illustrating the well-known fact that the hypertension associated with diffuse vascular disease is as a rule higher than that in glomerular nephritis.

Reference to the necropsied group (Table I) shows a significant parallelism between the arteriolar lesion in the kidney and that in the skeletal muscle. In six instances the muscle lesion was slight, rated one to two plus, whereas the kidney lesion in these instances was

severe. In 13 of the 24 cases, necrotizing arteriolar lesions were found in the kidneys. Twelve, or 50 per cent, of the patients died in uremia. This high incidence of uremia is greater than that found in hypertensive patients of all ages, and is due in our opinion (1) to the large percentage of negroes in the group and (2) to the fact that we deal only with patients dying under forty-six years of age. In other words, the high incidence of death from renal insufficiency here suggests that the arteriolar lesion in the kidney in the earlier decades of life and particularly in the negro race is more severe or pursues a more fulminating course than in the other vascular regions.

In the nonautopsied group (Table II) our observations on the arterioles of skeletal muscle were limited to the biopsy specimen. The frequency and severity of arteriolar lesions is apparent, for in only 3 cases were the lesions rated two plus or less by our criteria.

TABLE III

ARTERIOLES IN SKELETAL MUSCLE (BIOPSY AND AUTOPSY) AND IN KIDNEY IN 10 CASES OF HYPERTENSION, PATIENTS UNDER FORTY-FOUR YEARS

NAME	AGE	SEX	RACE	MUSCLE		KIDNEY	DEATH DUE TO
				BIOPSY	AUTOPSY		
C. G.	30	F	Black	3-4+	3-4+	4+	Uremia
E. W.	33	F	Black	3+	3-4+	3-4+*	Uremia
L. B.	35	F	Black	4+	3-4+	4+*	Uremia
M. G.	40	F	Black	3-4+	2+	2-3+	Cardiac
M. D.	41	F	Black	3-4+	3+	4+*	Uremia
M. D.	43	F	Black	4+	4+	†	Uremia
R. R.	27	M	Black	4+	4+	3-4+*	Uremia
J. S.	39	M	Black	3-4+	2-3+	4+*	Cardiac
W. J.	43	M	Black	2-3+	2+	4+*	Pneumonia
D. B.	33	F	White	3+	3-4+	3+	Cardiac

*Necrotizing arteriolar lesions.

†Autopsy restricted to thorax.

In Table III are data on 10 cases in which both a biopsy and an autopsy section of skeletal muscle were compared. This was done in order to check the reliability of our technical methods and also to study the question of whether or not the technic employed in removing a section of living muscle could introduce artefacts which might be interpreted as a lesion of the vessel wall. Our data show conclusively that the appearance of the arteriole in skeletal muscle in a biopsy specimen is practically identical with that seen in the autopsy specimen of the same case. It is apparent also that in this group the severity of the vascular lesion in the kidney agreed closely with that observed in both the biopsy and the autopsy specimen of skeletal muscle.

CONCLUSIONS

Observations on the foregoing group of cases appear to warrant these conclusions:

1. Arteriolar lesions in skeletal muscle are demonstrable in a high percentage of individuals dying under forty-six years of age of diffuse vascular disease with hypertension.

2. The severity of the muscular lesion in such cases usually parallels the severity of the arteriolar lesion of the kidney.

3. The arteriolar lesion in a biopsy specimen of voluntary muscle agrees closely in severity with that found in a post mortem specimen of the same muscle.

4. Our studies of blood vessels confirm the opinion reached some years ago from our clinical observations, that the vascular system of the negro is more vulnerable than the white man's to the noxious agent or agents responsible for the diffuse vascular lesions so often associated with chronic hypertension.

CIRCULATORY STUDIES ON A CASE OF ARTERIOVENOUS ANEURYSM

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THE deleterious influence of arteriovenous fistulas upon the heart was first demonstrated by Reid¹ in a series of interesting survival experiments on animals. Following the production of large arteriovenous communications in dogs, cardiac hypertrophy and dilatation and the evidence of myocardial insufficiency developed. This investigation was prompted by Reid's clinical experience with patients with arteriovenous aneurysms. In two such cases cardiac hypertrophy and dilatation had been noted by Osler and Halsted, but no causal relationship was considered.

The present knowledge of the pathological physiology associated with such fistulas is in large measure due to Reid,² Holman,³ Lewis and Drury,⁴ but certain of the phenomena associated with this interesting condition are still incompletely understood.

The results of the study of this case added a new observation to the published data regarding arteriovenous aneurysms. In general, our findings are in accord with the excellent clinical and experimental work of Holman, but differ in several respects from the investigations of Lewis and Drury.

CASE REPORT

The patient, a white male of twenty-three years, was shot in the right leg two years before. One bullet penetrated the anterior surface of the right lower leg over the tibia, and another entered the medial posterior portion of the right thigh and emerged laterally and posteriorly to the femur four inches above the knee. There was severe hemorrhage above the right knee at the time of the accident, enormous swelling of the thigh and shortly afterward the appearance of an ulcer on the anterior surface of the tibia where one of the bullets entered the leg. Since then the patient had been incapacitated because of pain and swelling of the injured leg. There had been some precordial pain, palpitation, effort dyspnea, and profuse sweating of the right leg.

When the patient was first seen the blood pressure was 130/60 mm. Hg, pulse 84, and temperature normal. There was moderate enlargement of the heart, confirmed by teleroentgenogram, and a soft systolic murmur at the cardiac apex.

The right leg was markedly edematous. There were numerous engorged, tortuous veins over the anterior surface of the right tibia and around the knee, and three ulcers in the skin of the lower portion of the right leg (Fig. 1). The right popliteal space was unusually full and pulsated with each heartbeat. The right femoral artery as it emerged beneath Poupart's ligament was markedly enlarged

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in comparison to the left femoral artery which was apparently normal in size. The right leg was swollen and wet with perspiration from the knee to the foot, while the left leg was dry. A marked systolic thrill was felt over the popliteal space, and a continuous roaring murmur with marked systolic intensification was heard over this area. Pressure sufficiently strong to obliterate the femoral artery caused an immediate drop in the pulse from 85 to 50* and the blood pressure rose on several occasions from 110/60 to 130/70 with disappearance of the thrill and murmur. It was clear from these facts that the patient had a fistulous communication between the popliteal artery and vein.



Fig. 1.—Popliteal arteriovenous aneurysm; duration two years.

As Lewis has stated that the sudden fall in the rate of the pulse when an arteriovenous aneurysm is occluded is of vagal origin,⁴ we administered atropine sulphate, gr. $\frac{1}{33}$, to paralyze vagus activity. In thirty minutes the maximum acceleration of the pulse occurred (rate 130), and the fistula was occluded by digital pressure. The pulse rate immediately fell to 114. An hour later with the rate 107, occlusion

*In a most interesting paper published in the Emanuel Libman Anniversary Volume, 1932. Dean Lewis discusses the history of "The Bradycardiac Reaction and the Cardiac Changes in Arteriovenous Aneurysms," and states that the bradycardiac reaction was first described by Nicolodoni in a congenital arteriovenous aneurysm, which he reported under the title of "Phlebarteriectasie der rechten oberen Extremität," in the Arch. f. klin. Chir. 18: 252, 1875. Fifteen years later Brasham described the same reaction in a traumatic arteriovenous aneurysm involving the femoral artery.

caused a decrease in pulse rate to 94. The blood pressure which was 122/80 mm. when the pulse rate was 107, rose 10 mm. in the diastolic reading following occlusion, while the systolic pressure was not influenced. This rise in diastolic pressure and stability of the systolic level persisted during the period of atropine influence.

That the blood pressure falls and the pulse rate increases immediately upon the opening of a large arteriovenous fistula, has been frequently demonstrated. Bainbridge⁶ has shown that increased venous return to the heart and, consequently, an increase in the pressure in the great veins and right auricle cause an acceleration of pulse rate, while Marey's law states that, other conditions remaining the same when arterial pressure is raised, the heart is slowed and vice versa, i.e., the pulse rate varies inversely as the arterial pressure.

The Bainbridge reflex is probably responsible for the acceleration of rate immediately after an arteriovenous fistula is opened. In all likelihood the reflex cardiac acceleration is caused by afferent impulses traveling up the vagi from the auricles and reducing the tone of the cardio-inhibitory center. The reduction of vagus tone, however, may occur from carotid sinns and aortic reflexes. The third possibility is the direct stimulation of the cardio-accelerator mechanism.

Lewis and Drury⁴ in summarizing their studies of five patients with arteriovenous aneurysm state that "the leak from artery to vein has no appreciable effect on general venous pressure," and "in those cases in which the arteriovenous anastomosis could be cut off at will this procedure failed to alter the venous pressure in measurable degree."

Our results were not in accord with these conclusions, and the readings of venous pressure obtained independently by different observers and by different methods were practically identical.

TABLE I
VENOUS PRESSURE DETERMINATIONS
(INDIRECT MEASUREMENTS)

	BEFORE OCCLUSION OF FISTULA	AFTER OCCLUSION
Left arm	57 mm. H ₂ O	62 mm. H ₂ O
Right arm	62 mm. H ₂ O	68 mm. H ₂ O
Right leg (above fistula)	62 mm. H ₂ O	
Right leg (below fistula)	60 mm. H ₂ O	85 mm. H ₂ O
VENOUS PRESSURE (DIRECT METHOD)		
	BEFORE OCCLUSION OF FISTULA	AFTER OCCLUSION
Left arm	60 mm. H ₂ O	95 mm. H ₂ O

The average increase in the venous pressure that followed digital occlusion of the fistula was 30 mm. of water.

From the theoretical standpoint it seems probable that the sudden diversion of a large amount of blood from the heart-artery-vena-cava circulation to the heart-artery-capillary-vein circulation would suddenly increase the volume of venous blood in the periphery and necessarily increase pressure. Harrison⁵ has proved that there is a very marked increase in cardiac output in animals with arteriovenous communications, and Holman has shown that the blood volume is greatly aug-



Fig. 2.

mented in the presence of large fistulous communications between arteries and veins. Thus the gradual dilatation and hypertrophy of the heart which occurs in the presence of large arteriovenous fistulas in human beings and in animals with large fistulas is explicable.

Fig. 2 shows the appearance of proximal and distal vessels and the arterial aneurysm opposite the fistula and Fig. 3 the successful extirpation of the arteriovenous fistula by Dr. Mont R. Reid. Following the operation the blood supply to the affected leg and foot improved im-

mediately, and in a few hours the pulsations in the dorsal pedis and posterior tibial arteries were readily palpable. Within a few days healing of the chronic leg ulcers began. There was a prompt and marked decrease in edema. The size of the heart showed a remarkable decrease (Figs. 4 and 5). This reduction in the cardiac diameter was probably dependent upon a decrease in the work requirements and in total blood volume. An immediate and permanent rise in diastolic pressure and a subsequent fall in the systolic pressure followed the opera-

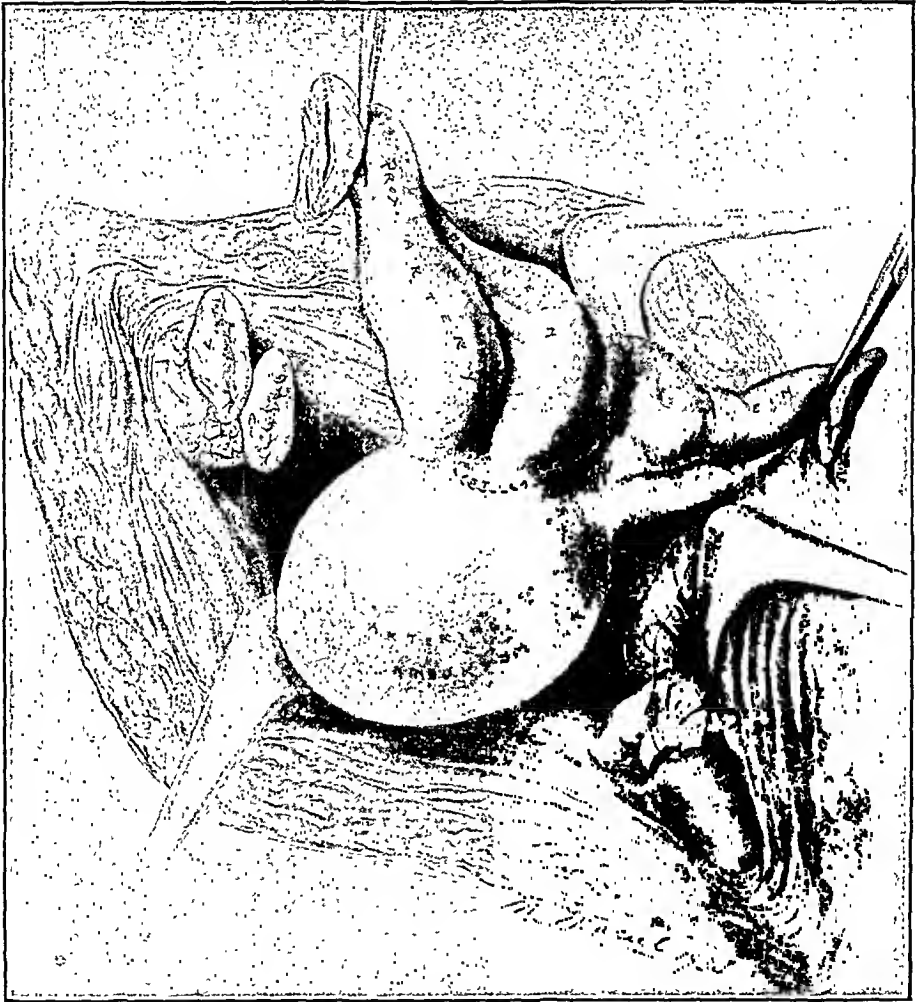


Fig. 3.

tion and were obviously consequent upon the replacement of normal peripheral resistance. The pulse rate returned to normal probably because of the abolition of an excessive return of venous blood to the heart. Associated with these circulatory readjustments the symptoms of myocardial insufficiency disappeared completely. The dilatation of the artery proximal to the fistula, in our opinion, has not been completely explained by Holman's hypothesis of compensatory dilatation because of increased blood volume flow; as the walls of the artery in our case were

thinner than normal, and there was a decided atrophy of the muscular elements of the arterial wall. Atrophy in a healthy structure in the presence of the necessity for increased work seems a biological paradox. Perhaps, as Reid believes, the lowered diastolic pressure in the proximal portion of the vessel decreases the blood supply to the walls of the artery, or the combination of the necessity of the vessel to carry a larger amount of blood without the requirement of the diastolic pressure usually maintained in large arteries may explain the mutation of the artery to a veinlike structure.

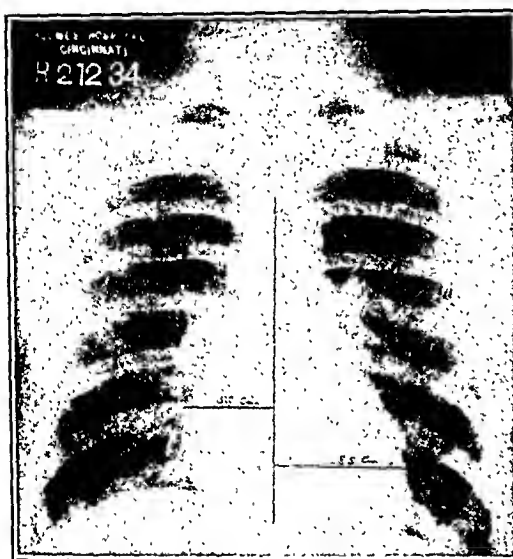


Fig. 4.

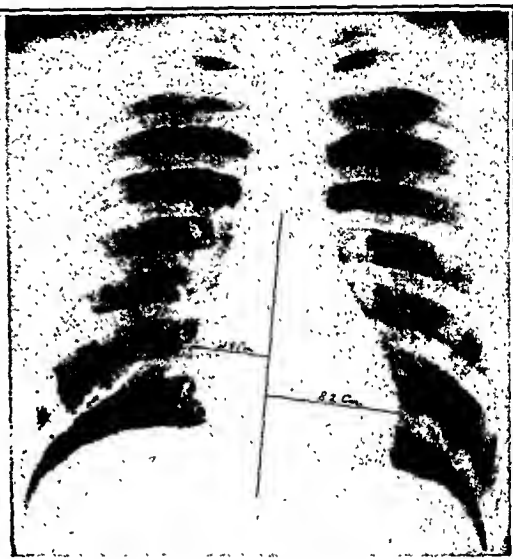


Fig. 5.

CONCLUSIONS

1. The establishment of a large arteriovenous communication between the popliteal artery and vein in a healthy young man was accompanied by: (a) an increase in systolic and a decrease in diastolic blood pressure levels; (b) cardiac and aortic dilatation and the symptoms of myocardial insufficiency; (c) dilatation and atrophy of the artery proximal to the arteriovenous communication, and hypertrophy of the vein in the area contiguous to the fistula, an arterial aneurysm opposite the fistula; (d) evidence of peripheral vascular malnutrition below the fistula, i.e., edema, ulceration of the skin, superficial varicosities, decrease in surface temperature, and decreased pulsation of the dorsalis pedis and posterior tibial arteries.

2. Digital occlusion of the fistulous communication produced: (a) bradycardia, and an immediate elevation of the diastolic and systolic arterial pressure; (b) definite elevation of the systemic venous pressure, i.e., antecubital vein; (c) slight decrease in the size of the heart as seen fluoroscopically.

3. Operative extirpation of the arteriovenous fistula caused: (a) the disappearance of symptoms of myocardial insufficiency; (b) a marked decrease in the size of the heart; (c) after the initial rise, a gradual drop in the systolic, and a permanent rise in the diastolic arterial blood pressure to normal levels; (d) diminution of peripheral edema in the affected leg, healing of the leg ulcers, the appearance of adequate arterial circulation in the foot.

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A CLINICAL AND PATHOLOGICAL STUDY OF CORONARY SCLEROSIS: ITS INCIDENCE IN HYPERTENSION AND ANGINA PECTORIS*

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WITH the focusing of attention upon disease of the coronary arteries in recent years, it has become evident, as the result of both clinical and autopsy studies, that the condition with which it is most often associated is arterial hypertension. At the autopsy table, coronary arteriosclerosis has been found in 90 per cent of hypertensive patients (Bell and Clawson¹) whereas in routine autopsies on individuals of all ages it occurs in from 25.9 per cent (Tery²) to 37.1 per cent (Allan³), and in from 39.6 per cent (Bell and Clawson¹) to 50 per cent (Rössle⁴) of persons over the age of forty-five years. There are in the literature few verified statements as to whether it may occur as an isolated phenomenon or more often concurrently with disease in other areas of the arterial bed. Bell and Clawson¹ found that in their series of hypertensive patients the frequency of renal arteriosclerosis in the coronary group was less than that in the "myocardial" and "encephalic" groups. Bork,⁵ on the other hand, believes that from the middle of the fourth decade of life a parallelism exists between arteriosclerosis of the coronary and peripheral arteries.

Clinically, such relationships are difficult to unravel because so often the symptomatology of coronary disease in essential hypertension is confused by the presence of a fatigued but adequately irrigated myocardium. The string galvanometer has proved of value in detecting myocardial damage consequent upon coronary narrowing or occlusion in arteriosclerotic heart disease, but the exact significance, as regards the condition of the coronary arteries, of many electrocardiographic abnormalities encountered in arterial hypertension demands further study.

We have investigated three groups of patients in an attempt to throw light upon the following questions.

1. What is the incidence of clinically detectable coronary sclerosis in essential hypertension?
2. What is the relationship, if any, between the occurrence of coronary disease and changes of the peripheral vessels, aorta and arterioles in this condition?

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3. What is the nature and significance of the electrocardiographic changes encountered in essential hypertension?

METHOD

The following groups of patients have been studied.

I. *Ninety persons with essential hypertension.* The incidence and distribution of clinically ascertainable vascular disease, in addition to the symptoms and signs (including routine electrocardiograms) of coronary sclerosis were determined. The peripheral vessels were palpated in all instances. The ocular fundi were examined. The status of renal function, as a measure of arteriolar disease of the kidneys, was determined by the following tests: (1) P.S.P.; (2) water test of Vollhard; (3) urea clearance; (4) level of urea in the blood; and (5) in many instances, the creatinine excretion test of Major and the renal test meal of Hedinger-Schlayer. Renal function was not considered to be impaired unless at least two of these tests gave abnormal results.

II. *Sixty-five hypertensive patients dying either of vascular disease or of unrelated causes.* The post-mortem incidence of coronary sclerosis was determined. Only an actual arteriosclerotic narrowing of the coronary vessels, with or without myomalacia or fibrous change of the myocardium, was regarded as significant. The clinical criteria, to be described later, for the presence of coronary sclerosis as applied to the first group were in this series checked against the post-mortem findings. The incidence of coronary change was correlated with that of arteriosclerosis of the aorta and arteriolar sclerosis of the renal vessels as determined by the microscope.

III. *One hundred and ten patients with angina pectoris, 10 of whom came to autopsy.* The incidence of peripheral and aortic sclerosis, together with the electrocardiographic findings, was contrasted with that in the preceding groups and with the findings in a series of 23 autopsied instances of coronary occlusion.

RESULTS

The essential data are given in Table I. Clinically, we have regarded the presence of angina pectoris, cardiac asthma, coronary occlusion, or, in their absence, electrocardiographic changes (to be discussed later) as presumptive evidence of coronary sclerosis. In the first group of 90 persons having essential hypertension such changes were encountered in 34 (37.7 per cent), distributed as follows: angina pectoris, 7 instances; cardiac asthma, 6 instances; coronary occlusion, one instance; electrocardiographic abnormalities only, 20 instances. The average age of these patients was slightly greater than that in the remainder of this series, and males were predominantly affected.

TABLE I
 DISTRIBUTION OF VASCULAR CHANGES IN ESSENTIAL HYPERTENSION, ANGINA PECTORIS, AND CORONARY OCCLUSION

DISTRIBUTION OF VASCULAR CHANGES IN ESSENTIAL HYPERTENSION, ANGINA PECTORIS, AND CORONARY OCCLUSION														
	HYPERTENSION (155 CASES)										CORONARY OCCLUSION (23 CASES)			
	CLINICAL				POSTMORTEM				ANGINA PECTORIS (110 CASES)				POSTMORTEM POSTMORTEM	
	WITH		WITHOUT		WITH		WITHOUT							
	CLINICAL	COR. SCL.	CLINICAL	COR. SCL.	CLINICAL	COR. SCL.	CLINICAL	COR. SCL.						
Number of cases	34	56	22-79	35	30	39-85	27-87	100	10	23				
Age, years	{ 45-90		57.8	63.0	61.9			31-88	55-85	40-76				
Sex { Male	19	18	18	24	17			60.5	66.8	63.0				
Female	15	38	38	11	13			55	7	16				
								45	3	7				

The average duration of elevated blood pressure (8.8 ± 1.0 year), according to the history in 20 instances, was significantly greater than the figure of 4.5 ± 0.7 year in 21 instances without evidence of coronary sclerosis. There is a statistically significant difference in the incidence of changes in the peripheral vessels, in the aorta (as determined by fluoroscopy), and in renal function in those patients with and without clinical evidence of coronary sclerosis. Widespread vasenlar damage is more evident in the group having coronary sclerosis. The series of patients with essential hypertension coming to necropsy was divided into two groups, depending on the clinical evidence of presence or absence of coronary sclerosis. The presumptive clinical evidence of coronary disease was distributed as follows: angina pectoris in 12 patients; cardiac asthma in 13; coronary occlusion in 7; electrocardiographic abnormalities only (from a total of 27 tracings) in 3 patients. Thus 35 patients, in a total group of 65, had clinical evidence of coronary disease. In 97 per cent \pm 2.8 per cent the clinical impression was substantiated by the post-mortem findings. There was one exception only, a patient with cardiac asthma whose coronary arteries were only slightly diseased. However, well-marked coronary sclerosis was present in over half (66.6 ± 8.5 per cent) of the patients who came to post-mortem examination in whom our clinical criteria for its presence were not met. Aortic sclerosis was significantly more common in the coronary group; whereas renal arteriolosclerosis, with the exception of one instance in which the kidney was not examined microscopically, was a universal finding.

TABLE II
PERCENTAGE OF DISTRIBUTION OF PERIPHERAL ARTERIOSCLEROSIS AND
ARTERIOLOSCLEROSIS

		HYPERTENSION—90 PATIENTS	
		WITH CLINICAL CORONARY SCLEROSIS 34 CASES	WITHOUT CLINICAL CORONARY SCLEROSIS 56 CASES
Peripheral arteriosclerosis	None	0.0 ± 1.7	28.3 ± 6.0
	Temporal	50.0 ± 8.5	39.6 ± 6.5
	Brachial	41.1 ± 8.4	20.7 ± 5.3
	Radial	79.4 ± 6.9	58.4 ± 6.5
	Dorsalis pedis	20.5 ± 6.8	22.6 ± 5.5
Arteriolosclerosis	None	5.8 ± 4.0	33.9 ± 6.3
	Fundi	76.4 ± 7.2	45.2 ± 6.4
	Kidneys	47.0 ± 8.5	22.6 ± 5.5

It is of interest to compare the above findings with those encountered in a group of patients with angina pectoris and with coronary occlusion. We again find a high incidence of peripheral, aortic, and renal arteriosclerosis, which is greater than might be expected, as a result of a complicating hypertension present in some of these patients.

One patient with angina pectoris and pernicious anemia, who came to autopsy, had unaltered coronary arteries and aorta. This is an exceptional instance and has been reported in detail elsewhere.⁶

The preponderance of males in these groups is in accordance with common experience.

In Table II the incidence and distribution of peripheral arteriosclerosis and arteriolosclerosis in patients with and without presumptive clinical evidence of coronary disease are listed. While we appreciate the difficulties in the clinical evaluation by palpation of the state of the arterial wall, it would seem that the data are sufficiently accurate satisfactorily to indicate a trend. These observations were made by each of us throughout, so that the subjective errors of interpretation should be uniform.

Thickening of the radial artery was encountered more often than changes in other vessels. This is contrary to pathological experience which teaches that the vessels of the leg and foot are more often and more intensively involved than those of the upper extremity. This is true both for medial calcification, a process which perhaps bears little relation to elevated blood pressure, and for intimal atherosclerosis where such relationship doubtless exists. The low incidence of change of the dorsalis pedis artery in these patients we believe is attributable to the difficulty in adequate interpretation of palpatory findings. Doubtless, atherosclerosis of this artery occurred more frequently than our fingers led us to believe.

The low incidence of changes of the vessels in the ocular fundi, as compared with that reported by other observers, requires a word of explanation. We disregarded minor variations, including only those instances in which we felt certain that the vascular changes were more intense and widespread than could be attributed to the aging process. Briefly, the criteria used were increased tortuosity and light refraction, together with arteriovenous compression, alone or combined with hemorrhage, retinal edema, or degenerative retinal lesions. The changes characteristic of malignant hypertension were not encountered in this group.

It is apparent from Table II that in this group of 90 patients with essential hypertension, clinically ascertainable coronary sclerosis was accompanied by widespread peripheral arteriosclerosis and, in most instances, arteriolar disease as well. No patient was encountered in whom there existed clinical evidence of coronary sclerosis, by our criteria, to the exclusion of evidence of disease in other areas of the vascular bed. The converse of this, however, was not true. There were many patients who apparently had generalized vascular damage without clinical evidence of coronary disease. The pathological data previously given suggest, however, that our clinical criteria were inade-

quate and that in all probability many of these patients had a significant degree of coronary sclerosis.

The above facts, if verified by further observations, may be of clinical value, as regards both diagnosis and prognosis of the cardiac status in patients with essential hypertension.

THE ELECTROCARDIOGRAM

The electrocardiographic abnormalities associated with coronary sclerosis need not be reviewed at this time. Suffice it to say that, in order of frequency, T-wave and R- or S-T changes in significant leads, left axis deviation, intraventricular conduction disturbances, including low voltage of the QRS complexes in all leads, large Q in Lead 3, and of the arrhythmias, extrasystoles, auricular fibrillation, partial or complete heart-block, and auricular flutter, are commonly observed.⁷⁻¹¹ However, certain changes are so often encountered in hypertension that, aside from the question of coronary involvement, it has been suggested¹² that they constitute a typical picture. These changes are left axis deviation, together with increased amplitude of QRS and a tendency for T to be directed oppositely to the major deflection. Master found these alterations in 33 of 152 hypertensive patients. They were for the most part instances of long standing hypertension, and, since the mortality was 40 per cent in three years, it would appear likely that coronary disease was present in many of them.

We have attempted to study the influence of high blood pressure upon the electrocardiogram by statistical analysis of the tracings obtained from two groups of patients, namely, 102 instances of essential hypertension and 87 instances of angina pectoris (Table III). No patient with acute coronary thrombosis was included. The first group was subdivided into patients with and without clinical evidence of coronary sclerosis. The anginal group, most or all of whom presumably had some degree of coronary disease, was subdivided according to the absence or presence of elevated blood pressure. The percentage incidence, with its standard deviation of the mean, has been tabulated for each group with the purpose of demonstrating which changes are significantly influenced by the presence or absence of increased blood pressure and of clinically evident coronary sclerosis. The following changes occurred too infrequently to allow of deduction: bundle-branch block; right axis deviation; inverted T₃; large Q₃; auricular fibrillation; extrasystoles. Table III discloses the following interesting facts.

Left axis deviation: This occurred more often in hypertension with clinical coronary involvement than without, but its incidence was not appreciably influenced by the presence or absence of elevated blood

TABLE III
ELECTROCARDIOGRAPHIC CHANGES IN HYPERTENSIVE PATIENTS WITH AND WITHOUT CLINICAL SYMPTOMS OF CORONARY SCLEROSIS CONTRASTED WITH THE CHANGES IN ANGINA PECTORIS

		ANGINA PECTORIS (87 CASES)				
		HYPERTENSION				
		WITH CLINICAL COR. SCL.	WITHOUT CLINICAL COR. SCL.	TOTAL	WITHOUT HYPERTENSION	WITH HYPERTENSION
		26	76	102	49	38
Number of cases						
No change	Per cent	23.0 ± 8.2	28.9 ± 5.1	27.4 ± 4.3	20.4 ± 5.6	13.1 ± 5.3
Left axis deviation	Per cent	57.6 ± 9.6	28.9 ± 5.1	36.2 ± 4.6	36.7 ± 6.8	42.1 ± 8.0
Right axis deviation	Per cent	7.6 ± 5.0	3.9 ± 2.2	4.9 ± 2.0	4.0 ± 2.6	2.6 ± 2.6
T ₁ diphasic or inverted	Per cent	34.6 ± 9.0	18.4 ± 4.1	22.5 ± 4.0	22.4 ± 5.9	50.0 ± 8.0
T ₂ diphasic or inverted	Per cent	26.9 ± 8.6	18.4 ± 4.1	20.5 ± 3.8	6.1 ± 3.3	44.7 ± 8.0
T ₁ + T ₂ diphasic or inverted	Per cent	23.0 ± 8.2	14.4 ± 3.8	16.6 ± 3.6	20.4 ± 5.6	13.1 ± 5.3
T ₃ diphasic or inverted	Per cent	7.6 ± 5.0	3.9 ± 2.2	4.9 ± 2.0	6.1 ± 3.3	23.6 ± 6.9
QRS change (all leads)	Per cent	15.3 ± 7.0	0.0 ± 1.0	3.9 ± 1.7	8.1 ± 3.8	5.2 ± 3.0
Bundle-branch block	Per cent	11.5 ± 6.0	1.3 ± 1.0	3.9 ± 1.7	0.0 ± 1.0	0.0 ± 1.4
Large Q ₃ { alone with other changes	Per cent	0.0 ± 1.7	1.3 ± 1.0	0.9 ± 0.3	4.0 ± 2.6	2.6 ± 2.6
	Per cent	11.5 ± 6.0	5.2 ± 2.4	6.8 ± 2.4	4.0 ± 2.6	2.6 ± 2.6
Auricular fibrillation	Per cent	7.6 ± 5.0	2.6 ± 1.7	3.9 ± 1.7	2.0 ± 2.0	13.1 ± 5.3
Extrasystoles	Per cent	15.3 ± 7.0	5.2 ± 2.4	7.8 ± 2.6	12.0 ± 6.6	0.0 ± 1.4

pressure in patients having angina pectoris. This finding is in accord with the experience of Ziskin¹³ who could not closely correlate the presence or absence of left axis deviation with the height of the blood pressure or the size of the heart, and concluded that hypertension alone does not produce preponderance. The high incidence of left axis deviation in our series of angina patients with normal blood pressures suggests that coronary disease may well be a factor in its production.

Diphasic or inverted T_1 or T_2 : The incidence of these abnormalities was apparently decidedly influenced by the presence of hypertension in our patients. T_1 or T_2 change occurred more frequently in those angina patients with hypertension than in those without; whereas the clinical presence of coronary disease in hypertensive patients increased its incidence but slightly as compared with the rest of the group. While the significance of this finding is not entirely clear, it would indicate caution in the interpretation of such changes, as regards the state of the coronary arteries, in the presence of hypertension.

Combined diphasic or inverted T_1 and T_2 : The incidence of this alteration was not increased by the presence of hypertension in the angina group, but was slightly greater in the hypertensive patients with clinical coronary disease. It seems that this change may safely be regarded as indicating the presence of coronary disease in these patients.

In summary, left axis deviation occurs more frequently in the presence of clinical symptoms of coronary sclerosis than in their absence. The presence of increased blood pressure plays little direct part in its production. Isolated changes of either T_1 or T_2 are common in arterial hypertension, and their significance, as regards the diagnosis of coronary artery involvement, is problematical. Changes of T_1 and T_2 together, however, cannot be attributed to the presence of hypertension alone. They probably indicate coronary damage.

SUMMARY

1. Clinically detectable coronary sclerosis occurred in 44.5 ± 3.8 per cent of 155 unselected hypertensive patients, distributed as follows: angina pectoris and cardiac asthma, each 12.2 per cent; electrocardiographic abnormalities only (from a total of 117 tracings) 19.6 per cent; coronary occlusion, 5.1 per cent.

2. In 65 hypertensive patients coming to necropsy, the clinical diagnosis of coronary sclerosis was substantiated in 97 ± 2.8 per cent of the instances in which the diagnosis was made. However, the condition was likewise present in 66.6 ± 8.5 per cent of the remaining patients in whom it was not suspected.

3. Coronary disease in these patients was almost uniformly accompanied by intense vascular changes in other areas of the vascular bed as disclosed by both clinical examination and post-mortem studies. The coronary arteries, however, were occasionally spared in instances of widespread vascular disease.

4. The electrocardiographic findings in this group of patients are contrasted with those encountered in patients having angina pectoris. The influence of uncomplicated hypertension and of coronary sclerosis upon the electrocardiogram is discussed.

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A CASE OF CONGENITAL COMPLETE HEART-BLOCK WITH LABILE VENTRICULAR RATE*

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THE failure of the slowed heart to respond to procedures paralyzing the vagus nerve endings has long been taught as demonstrating an intrinsic heart-block.¹ This has recently been called in question by the careful researches of Gilchrist, who showed that the adult heart with complete auriculoventricular block can accelerate on atropinization provided the drug is given in adequate dosage.² This same response to atropine was observed recently in the case of complete heart-block recorded here and regarded as congenital in origin. A similar lability of the ventricular rate characterized the response of this heart to fever, exercise, atropine and epinephrine.

The recent critical and analytical review of Yater, Lyon and McNabb³ and the inaugural thesis of Archigène⁴ serve as the chief guides to the literature on the subject of congenital heart-block. At the present a recapitulation of this material would be untimely. Interest in the case to be described seems to attach as much to the marked lability of the ventricular rate as to the rarity of the condition itself. It will be clear that if the stability of the pulse were to serve as the clue to the diagnosis of complete heart-block in this case, the diagnosis would not have been suspected. Leech⁵ in his proved case of congenital block likewise seldom found the same pulse rate at successive examinations. The comparatively high ventricular rate of juvenile block as compared to that of adult block has been commented upon by Clerc and Lévy.⁶ This again might serve to divert attention from the possibility of the diagnosis. Gilchrist⁷ feels that it is quite likely that at least some of these cases escape detection in childhood on account of the relatively fast ventricular rate. Clerc and Lévy⁶ believe that the rapid rate may explain why syncope is so rare in complete block in childhood.

A majority of writers^{4, 8-15} have found in cases of congenital complete heart-block that exertion of one form or another produces an acceleration of the heart rate of greater or lesser degree. Lian¹⁶ noted a transient acceleration of the heart and emphasized the importance of taking the rate during fractions of the first minute. Leech⁵ described an acceleration to 63 and noted that this response was thought to constitute evidence against the likelihood of there being

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a high degree of block, but a subsequent electrocardiogram showed complete auriculoventricular dissociation. Carter and Howland,¹⁷ McIntosh,¹⁸ Aylward,¹⁹ Anderson²⁰ and Sclar²¹ on the other hand found no change in heart rate to follow exercise.

Campbell and Suzman¹⁵ regard it as likely that chemical changes in the blood, especially the increased carbon dioxide content, are responsible for the increase in rate. That this may not be the entire explanation is attested by the response of some of the hearts of the type under consideration to nervous influences. Thus, whereas Whipple²² noted no respiratory variation in the ventricular rate, and neither Carter and Howland¹⁷ in their second case nor Fleming and Stevenson²³ in their first case found appreciable changes in the ventricular rate under vagal stimulation, D'Espine and Cottin²⁴ observed a reflex fall in heart rate from 28 to 24 on ocular pressure.* Leech⁵ also found a slight slowing from the oculocardiac reflex. Meyer,¹⁰ peculiarly enough, noted acceleration from 68 to 80 on ocular pressure, but there were extrasystoles.

The effect of atropine on hearts of this sort also has been studied by numerous workers, but unfortunately in many cases the dose given is not recorded.^{25, 26} Calandre,²⁷ Meyer,¹⁰ McIntosh,¹⁸ Davis and Stecher²⁸ and Brandenburg²⁹ noted the auricular rate to rise as it does in normal hearts, but they found no essential changes in the ventricular rate. On the other hand Pollak and Hecht,³⁰ Whipple,²² Smith,⁹ Leech,⁵ Aitken,¹³ Leaman,³¹ and Campbell and Suzman¹⁵ noted ventricular acceleration of variable degree, the maximal rise being observed from twenty to forty minutes after the injection.

That hearts showing congenital complete block can accelerate after epinephrine does not necessarily imply that purely nervous mechanisms are involved. This is amply demonstrated in the work of Cannon and his coworkers, who use the acceleration of the totally denervated heart to detect the presence in the blood stream of minute amounts of adrenin or adrenin-like substances. Thus, acceleration in congenital complete heart-block after epinephrine as described by Meyer,¹⁰ Leech,⁵ and Blackford and McGehee¹⁴ is not surprising. The failure of Fleming and Stevenson²³ to produce ventricular acceleration after 0.5 c.c. 1:1,000 epinephrine is probably without significance, for there was no simultaneous auricular acceleration.

The effect of fever in causing a rise in pulse rate has been described by a few authors.^{27, 11, 32, 28, 29}

These clinical observations find their counterpart in both anatomical and physiological investigations. Engel,³³ for example, has demonstrated the distribution of nerve fibers in the human heart to Purkinje tissue beyond the auriculoventricular node and the main bundle. Erlanger³⁴ found that whereas vagus stimulation usually caused no

*Case not electrocardiographically proved to be complete block.

change in the ventricular rate in complete block, in exceptional instances there was a minimal slowing. He also found the ventricular as well as the auricular rates in complete block to increase on stimulation of the accelerator nerve. Hering,³⁵ as well as Rijhl,³⁶ found that vagal stimulation caused slowing of the ventricles in experimental complete heart-block. It follows from the above review both clinical and experimental that there are both vagal and accelerator mechanisms which can alter the ventricular rate in complete heart-block.

REPORT OF CASE

The patient was a twelve-year-old schoolboy who was admitted on the medical service of the Peter Bent Brigham Hospital for sore throat and swollen neck glands of three weeks' duration. This began with a sense of irritation in the throat, soreness in the neck, fever, nausea, vomiting, vertigo, and headache. There was also some earache and dysphagia, but these cleared up after a week of bed rest only to return again with marked soreness of the throat and swollen, tender glands on both sides of the neck. Physical examination on admission showed a tall, angular, pale, and poorly nourished boy. The neck glands were large, tender and firm; the pharynx was markedly injected, and all the visible lymphoid tissue was swollen. The temperature was 102.2° F. and the pulse rate 80 beats to the minute. Chief interest centered in the heart. The left border of dullness was percussed 9 cm. to the left of the midsternal line in the fourth intercostal space. The apex impulse was diffuse, and a definite precordial wave, commencing near the nipple and moving toward the sternum with each systole, was caused by the cardiac impact. The first sound at the apex was snapping in quality and was followed by a moderate blowing systolic murmur which was heard well over the entire precordium. There was no cyanosis or clubbing of the fingers. The remainder of the examination, aside from a large scar on the right leg, was negative. On subsequent examination with the heart rate slower the systolic murmur was noted to be loudest in the lower precordium. There was occasionally heard in diastole a dull distant sound particularly well brought out after exercise or with the patient in the left lateral position. In addition there was noted an occasional change in the quality of the first heart sound which became higher pitched and louder.

On admission the white blood cell count was 22,700, the red blood cell count 4,310,000 and the hemoglobin 80 per cent (Sahli). The blood smear showed a differential count of 90 per cent polymorphonuclear leucocytes, 9 per cent lymphocytes, and 1 per cent basophiles. There was a slight "shift to the left." The urine contained the slightest possible trace of albumin by Heller's test, and the sediment was negative.

The temperature dropped to 99° F. by the third day but rose again to 100° F. concomitant with the development of a peritonsillar abscess, which caused the patient very little discomfort and ruptured spontaneously on the fifth day while he was eating lunch. The white blood cell count dropped to 12,700 on the sixth day. The pulse showed marked variations throughout his stay. On the second day it fell to 60, and it then varied around 50 but reached a level of 37 on his seventh day and again rose to 80 on the eighteenth day when the temperature was normal.

Numerous electrocardiographic tracings were taken. One on January 10, 1934, showed complete auriculoventricular dissociation with a ventricular rate of 46.7 and an auricular rate of 82.4. The auricles showed sinus arrhythmia. The complexes were upright in all leads. Tracings were not obtained at the times the heart rate

was 80 per minute. A roentgen ray film of the heart showed no cardiac enlargement or abnormality in contour other than a rather straight left border. The hilus shadows were slightly exaggerated. The diagnosis of congenital complete heart-block with probable interventricular septal defect was made.

The antecedent history of the patient was rather interesting. He weighed seven pounds at birth, and no cyanosis was noted at that time. He developed normally and was weaned at eleven months. At the age of two weeks he was examined by Dr. Karlton G. Percy of the Brookline (Mass.) Health Unit. He found the radial and apical rates to be 72 beats to the minute and noted a soft blowing systolic murmur heard best at the pulmonic area. His diagnosis was congenital heart disease. At the age of four the patient sustained extensive burns of his right leg; he was treated for this at the Children's Hospital with skin grafts, and he was followed at that institution as a case of congenital heart-block. He had pneumonia at the age of eight years and several attacks of asthma for which he was tested with negative findings. He gave no history of diphtheria, scarlet fever, rheumatic fever, or chorea. He had always been somewhat underweight and sickly, falling two years behind his classmates, but he was able to enter into practically all their activities. He never had syncopal or convulsive attacks. It is of interest that when treated at the Children's Hospital his pulse on admission was 135, then ranged between 53 and 90, the usual pulse being rather constantly at a level of 60.

During convalescence at the Peter Bent Brigham Hospital numerous studies were carried out. These included study of the effects of epinephrine, atropine, exercise, vagal pressure, carotid sinus pressure and ocular pressure. The ventricular as well as the auricular rates were accelerated after epinephrine, atropine, and exercise. The ventricular rate rose from 45.2 to a maximum of 74.3 beats per minute twenty-three

TABLE I
EFFECT OF EPINEPHRINE ON BLOOD PRESSURE, CIRCULATION TIME,
AURICULAR AND VENTRICULAR RATES*

ELECTRO-CARDIOGRAM	TIME	BLOOD PRESSURE	CIRCULATION TIME	AURICULAR RATE	VENTRICULAR RATE
1	Control (see upper tracing Fig. 1).	145/60	—	87.7	45.2
2	Determination of circulation time (0.25 c.c. 2 per cent sodium cyanide).	—	13 seconds	88.2	44.9
3	Five minutes after subcutaneous injection of 0.5 c.c. 1:1,000 epinephrine.	170/65	—	91.2	46.8
4	Seven minutes after injection.	170/60	—	96.6	47.4
5	Determination of circulation time (0.20 c.c. 2 per cent sodium cyanide).	—	9 seconds	100.3	51.4
6	Twenty minutes after injection (frequent extrasystoles).	180/60	—	117.6	62.6
7	Twenty-three minutes after injection. (See lower tracing Fig. 1.)	—	—	131.0	74.3
8	Twenty-six minutes after injection.	202/56	—	124.1	63.4

*I wish to thank Dr. M. A. Schnitker for assistance in carrying out this experiment.

minutes after the subcutaneous injection of 0.5 c.c. 1:1,000 epinephrine (Table I). At this time there were frequent extrasystoles, but the rate was counted in a strip in which there were no extrasystoles (Fig. 1). There was no change in the grade of block. The circulation time as determined by the sodium cyanide method fell from thirteen seconds to nine seconds seventeen minutes after the injection of epinephrine.

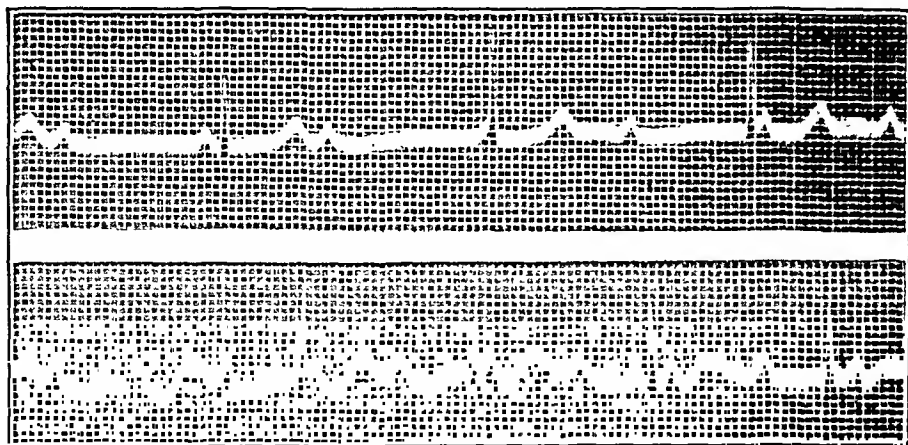


Fig. 1.—Electrocardiographic tracings taken before and twenty-three minutes after the subcutaneous injection of 0.5 c.c. 1:1000 epinephrine. Upper tracing (control) shows auricular rate 87.7 per minute and ventricular rate 45.2 per minute. Lower tracing shows auricular rate 131.0 and ventricular rate 74.3 per minute in a strip in which no extrasystoles are present. Both tracings are from Lead II.

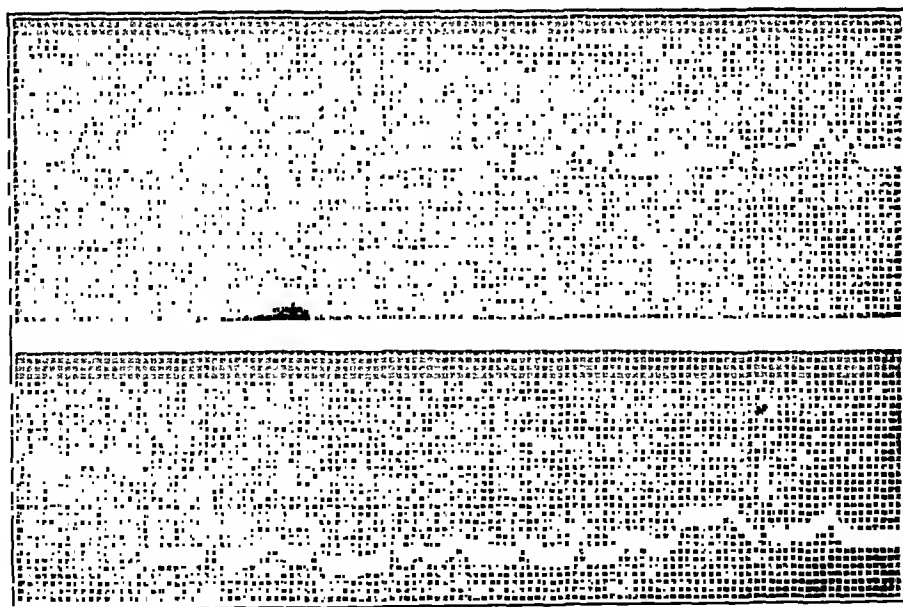


Fig. 2.—Electrocardiographic tracings taken before and one hour after the subcutaneous injection of 1 mg. of atropine sulphate. Upper tracing (control) taken from Lead II shows auricular rate 88.9 and ventricular rate 46.8 per minute. Lower tracing taken from Lead III shows auricular rate 107.9 and ventricular rate 59.1 per minute.

The ventricular rate rose from 46.8 to 59.1 beats per minute one hour after the subcutaneous injection of one milligram of atropine sulphate (Table II, Fig. 2). There is reason to believe that the rate might have been counted at a still higher level, if counts had been made at intervals during the first hour (see above). Exercise consisting of hopping alternately on each leg for three minutes caused a

slight transient acceleration of the heart rate, most apparent when the rate was counted each quarter-minute. During the first two quarter-minutes the calculated rates rose from 50 beats per minute to 56 beats per minute (Table III). While strong carotid sinus pressure or pressure on either vagus nerve lower down in the neck produced essentially no change in the rate, ocular pressure produced a slowing amounting to four beats per minute. There was no respiratory change in the ventricular rate.

TABLE II

EFFECT OF ATROPINE ON AURICULAR AND VENTRICULAR RATES

ELECTROCARDIOGRAM	TIME	AURICULAR RATE	VENTRICULAR RATE
1	Before injection (see upper tracing Fig. 2).	88.9	46.9
2	One hour after subcutaneous injection of 1 mg. atropine sulphate. (See lower tracing Fig. 2.)	107.4	59.1
3	Two hours after same.	68.3	42.8
4	Three hours after same.	63.7	34.8

TABLE III

EFFECT OF EXERCISE, CAROTID SINUS PRESSURE, VAGAL PRESSURE AND OCULAR PRESSURE ON THE HEART RATE

	RATE BEFORE EXERCISE	RATE BEFORE CAROTID SINUS PRESSURE		RATE BEFORE VAGAL PRESSURE		RATE BEFORE OCULAR PRESSURE	
		Right	Left	Right	Left	Right	Left
First quarter minute	13	11	11	12	12	12	12
Second quarter minute	12	11	11	12	12	12	12
Third quarter minute	13	11	11	12	12	12	11
Fourth quarter minute	12	12	11	12	12	12	11

	RATE AFTER EXERCISE	RATE DURING CAROTID SINUS PRESSURE		RATE DURING VAGAL PRESSURE		RATE DURING OCULAR PRESSURE	
		Right	Left	Right	Left	Right	Left
First quarter minute	14	11	11	12	12	11	11
Second quarter minute	14	12	11	12	12	11	10
Third quarter minute	12	11	11	12	11	11	10
Fourth quarter minute	11	12	11	13	12	—	—
Fifth quarter minute	12	—	—	—	—	—	—
Sixth quarter minute	12	—	—	—	—	—	—
Seventh quarter minute	13	—	—	—	—	—	—
Eighth quarter minute	13	—	—	—	—	—	—

SUMMARY

A case is described of congenital complete heart-block with probable interventricular septal defect, seen during an attack of acute tonsillitis. The ventricular rate varied spontaneously and with fever, exercise, ocular pressure, and the administration of atropine and epinephrine. The subject of the lability of the ventricular rate in congenital complete heart-block is discussed.

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Department of Clinical Reports

INTRAPERICARDIAL RUPTURE OF AORTA

REPORT OF TWO CASES

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NO ATTEMPT will be made to review the literature on this very interesting subject. A review of the first case reported makes one wonder how early in life degenerative changes may be expected. It is unfortunate that the clinical study of this patient is so limited, but he was not admitted to the hospital, as the seriousness of his illness was not suspected.

CASE 1.—G. H. H., white male, aged nineteen years, well-developed young athlete and student in the Citizens' Military Training Camp, Fort Snelling, Minnesota, August, 1932. He was an excellent tennis player and had reached the semi-finals in doubles and singles in the C. M. T. C. tournament when he was forced to withdraw because of very severe precordial pain on August 21, 1932. This severe pain was of short duration, but there was a persistent feeling of uneasiness with anxiety that was progressive up to the fatal termination.

His mother and father both have arterial hypertension.

Present Illness: August 23, 1932, about 7 P.M., while in a stooping position washing his clothes, he was conscious of a sharp, cracking sensation in his chest. This was, however, not complained of until one hour later when he complained of pain in his right chest, dyspnea and anxiety. Examination by a doctor showed temperature normal, pulse 80, respiration 22. During the night he was uncomfortable, slept very little, and the pain in right chest continued. He remained in quarters August 24 with the same symptoms and pain prevailing. Appetite was nil. He again spent a very restless, anxious night. On the morning of August 25 he was up by 6 A.M., and still complained of pain in his chest. He was instructed to remain in his barracks for the day, where at 8:55 A.M. he was found lying across his bed unconscious, after having taken a gun out of a rack for another student. There was marked cyanosis of face and hands, and respiration was labored. He was soon seen by several of the Camp physicians and at 9 A.M. was pronounced dead. Apparently this exertion completed the rupture of the aorta, with the resultant intrapericardial hemorrhage.

Personal History: He had the usual childhood diseases without complications. Had never had any prolonged illness. No operation of any kind. Always healthy, was an excellent athlete, playing baseball, basket-ball, football and tennis. Denied venereal diseases.

An autopsy done by Major T. W. O'Brien, M. C., showed the following: "The pericardium is distended and filled with blood (about 200 c.c. in amount) due to a rupture of the ascending aorta. The heart is in firm contraction, normal in size with a well-developed left ventricle. There is a rupture in the ascending

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aorta, extending in an irregular, longitudinal direction upward from a point just above the right coronary artery for a distance of 3 inches. The tear in the intima was definitely older than that in the adventitia, which apparently occurred several days later after the blood had dissected posteriorly between the intima and adventitia. The rupture in the adventitia was distal to the rent in the intima. From the appearance of the dissecting hemorrhage one would believe it to be probably several days old. No other pathological lesion of importance was found elsewhere."

Microscopic Report: (Made by Major P. E. McNabb, Medical Corps.) "Sections made through the aorta at a point some distance from the rupture show a mild separation of the tissue elements in the media. The adventitia is thickened both by increased fibrous tissue and by edema. There is no recent in-



Fig. 1.

flammatory reaction in the region. The section taken from near the point of rupture shows degeneration in the media, but the adventitia is widely separated from the media by a massive hemorrhagic infiltration. This appears to be of different ages, and in many areas the clot contains numerous leucocytes and a large amount of blood pigment. In the adventitia there is both diffuse and localized infiltration of leucocytes. The most conspicuous change, however, occurs in the endothelium of the blood vessels. One of the sections shows a longitudinally directed vessel in which the endothelium is remarkably swollen, proliferating, and in some areas appears to have two or three rows of cuboidal shaped cells. Some of these enlarged endothelial cells are detached into the lumen of the vessel."

CASE 2.—J. W. L., white male, aged fifty-five years, was admitted to Fitzsimons General Hospital March 27, 1934, with the following history:

Symptoms and Complaints: Coughing and expectorating blood. Face, lips and finger tips cyanotic. Pain, severe, in the left chest; weakness and cardiac distress on respiratory movement. Marked insomnia for two days.

Present Illness: The patient was in good health until March 25, 1934, when he was defrosting a refrigerator and was seized with a sudden, severe, cardiac pain, as if he had been shot. Respiration increased this pain, and he had to be assisted to a chair where he soon fainted and fell to the floor. When he revived he felt weak and cold, and still had the severe pain in the left chest. The family physician soon was called in, and he felt there was some coronary disease. His general condition remained much the same until he was admitted to this hospital on the afternoon of March 27, 1934.

Personal History: Herniotomy, left, 1919, with recurrence several years later. Hemorrhoidectomy and tonsillectomy, 1927. Second repair of hernia, left, January, 1934. The last operation was apparently successful and recovery was uneventful. Always enjoyed good health; no change in weight; denied venereal diseases (Wassermann negative at this hospital in 1927), and family history was essentially negative.

Condition on Admission: Pulse 108, temperature 99° F., respiration 26. A well-developed, white male with good nutrition, weighing about 175 pounds. Face, lips and finger tips cyanotic. Coughing moderate, with some expectoration of blood. Pupils equal in size, active to light. Reflexes considered as normal. Blood pressure 190/120 mm. White blood count 14,000 with 89 per cent of polymorphonuclears.

An x-ray film made soon after admission was reported as follows: "Bedside x-ray examination of the chest shows the thorax negative. Trachea lies slightly to the right of the midline. Cardiac shadow is somewhat horizontal in shape and appears slightly enlarged to the left and right. There appears to be a considerable tortuosity of the thoracic aorta. A mottled, uneven clouding in the basal portion of the right lung is suggestive of a lung infarct. This lung is otherwise clear. The left lung is essentially negative."

An electrocardiogram made March 29 showed the following: "Auricular rate 107; ventricular rate 107; rhythm regular; left axis deviation; P₂ is diphasic; P-R interval is 0.10 sec.; QRS slurred in Lead III; S-T elevated (marked) in Leads I and II; depressed in Lead III; T-wave inverted, Lead III. The findings in this case suggest acute coronary thrombosis with severe myocardial damage."

The patient's general condition remained about the same while he was in the hospital until the morning of March 31, 1934. While he was eating his breakfast, the nurse left the room for a few minutes, and on her return she found him dead.

The autopsy, made by Major H. P. Sawyer, M. C., follows: "The heart is huge and on palpation appears to be solid. The pericardium is so thick that one cannot see the color of the blood through it. On opening the pericardium a huge clot is found surrounding the entire heart, extending up to the great vessels and about 900 c.c. in amount. The pericardium at about the auriculo-ventricular septum shows a line of old visceroparietal adhesions. Above this old line the clot seems older and is firmer and more fibrous. The lower portion of the clot is more recent and more fluid. The right heart is fairly normal, the muscle pale but firm. The valves are all normal. The right ventricle appears as if plastered over the right side of the globular, hypertrophied left ventricle. The latter is about 2.5 cm. in thickness. The mitral valves appear competent. Following up the aorta about 3 cm. above the sinuses of Valsalva there is a long rupture which is directed upward and a little to the right. The aorta shows a moderate sclerosis from the summit of the arch down to the bifurcation, but at the rupture there is very little sclerosis. At the point of rupture the wall is

a little thinner than elsewhere. There is a noticeable fatty infiltration of the media in the sclerotic areas. The coronaries show a moderate amount of sclerosis, but there is no occlusion. The impression is that a small rupture occurred first on exertion, the resulting hemorrhage into the pericardial sac being confined for the time being to the upper third of the sac by the line of adhesions along the auriculoventricular septum. Later the primary rupture enlarged, due to pressure, the retaining line of adhesions gave way, and the entire sac filled to extreme distention."



Fig. 2.

Microscopic Report of Aorta: "Sections made at the site of rupture show the elastic fibers of the media, which are markedly decreased in all sections, are still more infrequent as the line of rupture is approached. Both elastica interna and externa are either totally absent or so thin as to be unrecognizable. There is a noticeable infiltration of the media with fat and a definite degeneration of all the medial elements. There also appears a large, misplaced branch of the vasa vasorum which occupies the medial portion of the section and in one place bulges the interna markedly. The tear in the artery traverses the vascular appearing space, which practically halves the thickness of the wall."

This second case is especially interesting in that the recorded damage as shown by the electrocardiograph resembled that of acute coronary thrombosis. It is believed that this may have been due to the pressure of the tensely distended pericardial sac upon the coronary branches, resulting in ischemia of the heart muscle.

These cases are reported chiefly to show that degenerative changes of the cardiovascular system may be present in youth. It is possible that they are much more prevalent than is believed. In the case of the C.M.T.C. student the violent exercise apparently caused death in a person who possibly might have lived out the average span of life had he not been such an ardent participant in strenuous sports.

Society Transactions

AMERICAN HEART ASSOCIATION, 1934

THE tenth annual scientific session of the American Heart Association was held on June 12, 1934, at the Hotel Cleveland, Cleveland, Ohio, with Dr. Harold E. B. Pardee as presiding officer. The following program was presented.

Program

Pathology of Coronary Sclerosis. Timothy Leary, M.D., Boston, Mass. See page 328.

Coronary Spasm as a Possible Factor in Producing Sudden Death. Timothy Leary, M.D., Boston, Mass. See page 338.

Coronary Arteriosclerosis, Coronary Thrombosis, and the Resulting Myocardial Changes. I. Anatomical Lesions. Otto Saphir, M.D., Walter S. Priest, M.D., Walter W. Hamburger, M.D., and Louis N. Katz, M.D., Chicago, Ill. To be published in a later issue of the AMERICAN HEART JOURNAL.

A Clinical and Pathological Study of Coronary Sclerosis: Its Incidence in Hypertension and Angina Pectoris. F. R. Nuzum, M.D., A. H. Elliott, M.D., and R. D. Evans, M.D., Santa Barbara, Calif. See page 367.

The Relation of Coronary Arteriosclerosis to Auricular Fibrillation With Special Reference to the Term "Arteriosclerotic Heart Disease." Morton G. Brown, M.D., and Samuel A. Levine, M.D., Boston, Mass.

ABSTRACT

An analysis was made of all cases with auricular fibrillation which came to post-mortem examination at the Peter Bent Brigham Hospital, exclusive of those with known rheumatic valvular disease. Significant disease of the coronary arteries, although fairly frequent among those with hypertension, was not usually the sole factor in the development of permanent fibrillation. Hypertension was an etiological factor in 63.8 per cent of the cases with permanent fibrillation, and in 67.8 per cent of those with transient fibrillation. Evidence is presented that marked peripheral arteriosclerosis of itself need be no indication that the coronary arteries are sclerosed, or that the efficiency of the heart is in any way altered. From this, we therefore suggest that the term "arteriosclerotic heart disease" should be given up entirely or clarified in its expression.

The Relation of Arteriosclerosis to Hypertrophy of the Heart. James G. Carr, M.D., Chicago, Ill.

ABSTRACT

This paper is based upon a study of 351 autopsy reports from the Cook County Hospital. These reports are studied in four groups: (1) a group with cardiac hypertrophy in which cardiac disease was the cause of death; (2) a group in which cardiac hypertrophy was present as an incidental finding; (3) a group in which severe coronary sclerosis was accepted as the principal disease; (4) a group in which generalized arteriosclerosis was incidental, in a very few of these cases the arteriosclerosis was regarded as the principal disease. Group 4 includes no reports considered in the other groups. No reports are included in which the cardiac enlarge-

ment could be attributed to valvular or renal disease. An attempt is made to evaluate arteriosclerosis, general or especially pronounced in the coronary vessels, as a factor in the production of cardiac hypertrophy. Thus far the study does not support the view that arteriosclerosis is a cause of cardiac hypertrophy.

Arteriosclerotic Heart Disease: Coronary Thrombosis and Its Effect on the Size of the Heart. Emmet F. Horine, M.D., and Morris M. Weiss, M.D., Louisville, Ky.

ABSTRACT

Statements have been made that coronary thrombosis of itself may produce cardiac enlargement. Patients with arteriosclerotic heart disease and normal sized hearts who developed coronary thrombosis were followed for varying intervals of years. None developed cardiac enlargement. Heart-block, arteriosclerotic in origin, did not produce cardiac enlargement. Autopsy studies and a brief summary of pertinent literature are included.

Arteriosclerotic Heart Disease in Diabetes. H. F. Root, M.D., and T. P. Sharkey, M.D., Boston, Mass.

ABSTRACT

The frequency and severity of arteriosclerotic heart disease as demonstrated by autopsy examinations at the New England Deaconess Hospital were correlated with the clinical records, special attention being given to the etiological factors of hypertension, obesity, and duration of diabetes. One-half the patients had had hypertension. The symptomatology and clinical course of the cardiac cases were characteristically those of insufficiency of the coronary circulation, with a high incidence of acute coronary thrombosis as a cause of death. The severity of coronary disease was greater in the hypertensive group, but the incidence of arteriosclerotic gangrene of the feet was less affected by hypertension. Absence of marked hypertrophy of the heart, even in the presence of hypertension together with a high incidence of myocardial degeneration, was noted. Distinction between arteriolar sclerosis and large vessel sclerosis was not clear-cut because of the coexistence of both types. The evidence indicates that arteriosclerosis is unimportant as a cause of diabetes, but the development of arteriosclerotic heart disease in diabetic patients is excessive.

Valvular Atherosclerosis. Sylvester McGinn, M.D., and Paul D. White, M.D., Boston, Mass. To be published in a later issue of the AMERICAN HEART JOURNAL.

Coronary Arteriosclerosis, Coronary Thrombosis and the Resulting Myocardial Changes. II. An Evaluation of the Clinical Pictures Including the Electrocardiographic Records Based on the Anatomical Findings. Walter S. Priest, M.D., Walter W. Hamburger, M.D., Louis N. Katz, M.D., and Otto Saphir, M.D., Chicago, Ill. To be published in a later issue of the AMERICAN HEART JOURNAL.

Significance of the Coronary Circulation in Arteriosclerotic Heart Disease. Fred. M. Smith, M.D., W. D. Paul, M.D., Iowa City, and H. W. Rathe, M.D., Waverly, Iowa.

ABSTRACT

This report is based on the study of approximately 400 cases of arteriosclerotic heart disease in which there was a significant involvement of the coronary arteries. Forty-five of these cases came to necropsy. The progress of the cardiac disability was analyzed with reference to the vague clinical manifestations and their relationship to possible disturbance in the coronary circulation. We have been par-

ticularly interested in the incidence of suspected and unmistakable coronary accidents, the significance of paroxysmal dyspnea and the relationship between angina of effort and coronary occlusion. Most of these patients were studied electrocardiographically, and many had serial curves. This study emphasizes the importance of constantly bearing in mind the status of the coronary circulation in arteriosclerotic heart disease. In the patients who came to necropsy there was, in general, a close correlation between the clinical interpretation and the pathological findings.

Mechanism of Pain Production in Angina Pectoris. Louis N. Katz, M.D., Chicago, Ill. See page 322.

Anginal Pain and Coronary Disease: A Clinical and Pathological Study of 500 Cases. Kenneth B. Turner, M.D., Howard G. Brunn, M.D., and Robert L. Levy, M.D., New York, N. Y.

ABSTRACT

This series of cases has been analyzed with cardiac pain as the central point of interest, in an attempt to correlate the clinical aspects and the pathological anatomy. Various etiological types and degrees of coronary artery disease have been considered. Such factors as the location of the lesions, character and extent of myocardial involvement, associated clinical and pathological states and causes of death are discussed. The circumstances which favor the occurrence of anginal pain are described.

The Relation of Symptoms of Cardiac Infarction to the Pathological Findings. Nathan S. Davis, III, M.D., Chicago, Ill.

ABSTRACT

An analysis of the records of 77 successive cases of cardiac infarction has been made. Pain was present in about 48 per cent, absent in about 33 per cent, and in 18 per cent there was no history. In the group with pain, epigastric pain was present in about 14 per cent, nocturnal angina in 8 per cent, and about 35 per cent had had previous anginal attacks. Nocturnal dyspnea, paroxysmal dyspnea, and congestive heart failure were more common in the group without pain, as were also cardiac dilatation and cardiac aneurysm. Occlusion of the circumflex branch of the left coronary artery was found most often in those patients without history; occlusion of the descending branch in those with and without pain. Stenosis and occlusion in one branch or stenosis in one and occlusion in another occurred most often in those with pain, least often in those without. Myomalacia, hemorrhagic, irregular and multiple areas of infarction are relatively more common in those with pain; recent and ancient fibrosis, anemic and circumscribed areas of infarction in those without pain.

Factors Which Obscure Electrocardiographic Diagnosis and Localization of Acute Myocardial Infarction, and Recent Observations Permitting Greater Accuracy of Diagnosis. A. R. Barnes, M.D., Rochester, Minn.

ABSTRACT

Analysis of a large series of cases of acute myocardial infarction reveals several factors which interfere with the development of typical electrocardiographic changes. These factors are discussed and illustrated. The importance of observing the electrocardiographic changes in the initial ventricular complex, and especially the value of the combined study of the initial and final ventricular complexes, is stressed. The electrocardiographic pattern which may develop when acute coronary occlusion is complicated by pericarditis is pointed out. The interpretation of minimal electro-

cardiographic changes of infarction is discussed. The supplementary information obtained under such conditions by the use of anteroposterior thoracic leads is illustrated.

Localization of Cardiac Infarcts According to Component Ventricular Muscles.

Jane Sands Robb, M.D., J. G. Fred Hiss, M.D., and Robert C. Robb, Sc.D., Syracuse, N. Y. See page 287.

Electrocardiograms in Coronary Sclerosis and Occlusion. Howard B. Sprague, M.D., and Edward S. Orgain, M.D., Boston, Mass.

ABSTRACT

This study correlates the electrocardiograms taken during the course of acute coronary occlusion with the pathological findings. A similar correlation is made in a series with diffuse myocardial change with or without evidence of old myocardial infarct. A third group has been studied in which the autopsy findings revealed advanced coronary sclerosis but in which the electrocardiographic findings were equivocal. Electrocardiograms of patients with coronary arteriosclerosis but without cardiac infarction may provide very indefinite evidence of the severity of the process.

Changes in the Electrocardiogram Resulting From Induced Attacks of Angina Pectoris. Merritt B. Whitten, M.D., and James H. Herndon, M.D., Dallas, Texas.

ABSTRACT

Electrocardiograms were taken on a number of patients before and during attacks of angina pectoris induced by exercise. Striking changes in the electrocardiogram, especially in the Q-wave, RS-T interval and T-wave, were observed in a number of the cases. Others showed only slight changes in the Q- and T-waves and RS-T interval. Control patients were studied to determine how slight a change in the various waves and intervals of the electrocardiogram might be considered significant following exercise similar to that producing the anginal attacks. Control cases included (1) patients with typical history of angina pectoris, but in which we failed to precipitate anginal pain on exercise, (2) patients exhibiting heart disease other than that involving the coronary arteries, and (3) patients with apparently no organic heart disease. A study of the electrocardiograms in these control cases seemed to indicate that slight changes in the electrocardiogram occur with exercise even in the absence of angina pectoris.

Observations on Prognosis in Angina Pectoris. A. M. Wedd, M.D., and R. E. Smith, M.D., Clifton Springs, N. Y.

ABSTRACT

The paper is based on the records of 165 cases of angina of effort, seen in a clinic in which arteriosclerotic heart disease is the predominant type. The influence of hypertension, obesity, familial vascular disease, and certain miscellaneous factors has been considered. Electrocardiograms were available in most cases but were found of no value for prognosis. One-third of these patients died suddenly, and over one-half died of coronary occlusion. The duration of life in this series was greater than is usually anticipated. While prognosis in the individual case must always be uncertain, because of the long duration and the late ages of onset and death compared with life expectancy, the anginal syndrome does not stand out as a serious complication of arteriosclerotic heart disease.

Observations on the Pathology and Pharmacology of Syncope and Sudden Death in Coronary Disease. M. H. Nathanson, M.D., Minneapolis, Minn.

ABSTRACT

An analysis of 142 necropsy records of patients who had had coronary disease terminating in sudden death indicated that a structural basis for the sudden death is infrequent. The effect of drugs upon the two mechanisms within the heart which may cause a sudden cessation of circulation, i.e., ventricular fibrillation and ventricular standstill, was studied in human subjects. The cardiac standstill induced by carotid sinus pressure could be prevented by a large number of compounds, all related in structure to epinephrine. The preponderance of evidence indicates that ventricular fibrillation is usually the underlying mechanism in sudden cardiac death. Ventricular rhythms of a prefibrillation type were induced by intravenous injection of epinephrine and the effect of various drugs investigated. Quinidine prevented the development of these rhythms in ten subjects. The action of ergotamine, potassium salts, sodium amytal and acetyl-B methylcholin was studied in a smaller group of cases. By utilizing the carotid sinus reflex, quinidine was found to possess a vagoparetic action and thus would also have a tendency to prevent vagal inhibition of the heart.

Treatment of Various Forms of Arteriosclerotic Heart Disease by Means of Total Ablation of the Normal Thyroid Gland. David Davis, M.D., A. A. Weinstein, M.D., J. E. F. Riseman, M.D., and H. L. Blumgart, M.D., Boston, Mass. To be published in a later issue of the *AMERICAN HEART JOURNAL*.

Theophyllin in the Treatment of Arteriosclerotic Heart Disease. Fred M. Smith, M.D., W. D. Paul, M.D., Iowa City, and H. W. Rathe, M.D., Waverly, Iowa.

ABSTRACT

Theophyllin in the form of theophyllin ethylenediamin has been employed at the University Hospital for the past seven years in the treatment of arteriosclerotic heart disease. This medication was often continued after the patient was discharged from the hospital, and in certain instances it was taken over a period of several weeks or months. Frequently these patients reported that they were progressing very satisfactorily, but soon after the drug was discontinued the symptoms returned. This study also includes observations on a series of approximately 100 patients who were not hospitalized. In the majority of these, theophyllin was the only cardiac drug employed. This series consisted of patients presenting varying degrees of dyspnea including the paroxysmal type (some with extensive edema), angina of effort, and coronary occlusion. Our observations have convinced us that theophyllin is a valuable remedy in the treatment of arteriosclerotic heart disease.

Tolerance to Digitalis in Patients With Normal Hearts and in Those With Arteriosclerotic Heart Disease. Thomas M. McMillan, M.D., Samuel Bellet, M.D., and William E. Robertson, M.D., Philadelphia, Pa. To be published in a later issue of the *AMERICAN HEART JOURNAL*.

(Papers read by title)

The Chemistry and Morphology of Normal and Atheromatous Aortas. Pearl M. Zeck, M.D., Cincinnati, Ohio.

ABSTRACT

Over 20 sections on nonsyphilitic aortas, ranging from the normal to markedly sclerotic ones, have been analyzed quantitatively for lipoids, a small portion of each also being sectioned for microscopic study, and lantern slides prepared. The lipid

percentages include those for total cholesterol, free cholesterol, cholesterol esters, fatty acids, and lecithin, the methods used being essentially those of Dr. Bloor of Rochester, N. Y. Graphs are being drawn to show the relationship between the degree of atheroma and the percentages of the various lipid substances.

Arteriolar Lesions of Skeletal Muscle in Hypertension. R. W. Scott, M.D., David P. Seecof, M.D., and A. A. Hill, M.D., Cleveland, Ohio. See page 355.

How Often Is Arteriosclerotic Heart Disease an Isolated Arteriosclerotic Manifestation? Edward W. Hollingsworth, M.D., and W. L. McNamara, M.D., Hines, Ill.

ABSTRACT

The diagnosis of arteriosclerotic heart disease was considered established when there were the usual findings of myocardial disease and when syphilis, rheumatic fever, hypertension and sepsis could be ruled out. Slides of the various tissues were examined and changes noted in the thickness of the walls of the arteries, which were divided roughly into large and small. The dividing point in our classification was about 75 microns. Because of distortion in sections, including collapse and shrinkage, the ratio between wall and lumen was not employed. Routine formalin fixation was employed. In practically every case there was sclerosis in organs other than the heart. In the heart itself the large vessels were more frequently and more severely affected than the small. Both large and small kidney vessels were affected in practically every case, and about equally; the same applies to the spleen. The vessels of the other organs—adrenals, pancreas, brain, and lungs—in the order named, were less often and less severely involved. These findings are, in general, in agreement with those of other writers, excepting that there was no marked difference between frequency or severity of involvement in small and large arteries.

Observations on the Clinical Course of Arteriosclerotic Auricular Fibrillation. Louis F. Bishop, M.D., and Louis F. Bishop, Jr., M.D., New York, N. Y.

ABSTRACT

Sixty-eight patients with arteriosclerotic auricular fibrillation who had been followed in practice for a number of years were studied. Paroxysmal and chronic fibrillation are separately considered. A subdivision is made into arteriosclerosis with and without hypertension. Age, sex, symptomatology, and mode of treatment with particular regard to digitalis and exercise, are reviewed. The clinical course of these patients is analyzed as to their physical activity, occurrence of embolism, onset of congestive failure, and duration of life.

The Value of the Electrocardiogram in Interpreting Coronary Disease. Louis N. Katz, M.D., Anne Bohning, M.D., Chicago, Ill., and Harry Landt, M.D., Cincinnati, Ohio.

ABSTRACT

In only five of more than 100 cases diagnosed clinically as advanced coronary sclerosis were the four leads found to be normal, but never, as yet, after a recent coronary occlusion (more than 50 cases). In some of these latter the characteristic changes appeared only in Lead IV. The use of frequent serial four-lead records has been of assistance in differentiating between anginal attacks and myocardial infarction, and in determining whether the coronary sclerotic process is rapidly progressive or relatively stationary. Exercise was found to produce changes in the four leads in proportion to the degree of impairment of the coronary circulation.

An analysis of the standard three leads of our records of recent coronary occlusion shows that mixed T types often occur and occasionally the changes in Lead I and Lead III are in the same direction. These types fall into: (1) the indeterminate, (2) T_n and (3) T_p types. Positive coronary T-waves may be the dominant alteration on occasion instead of the negative coronary T-wave. In a small series of cases (seven) checked by autopsy, Lead IV was useful in differentiating anterior from posterior infarcts, even when the ordinary leads were misleading or not characteristic.

The Effect of Theophyllin Ethylenediamin on Experimentally Induced Cardiac Infarction in the Dog. W. M. Fowler, M.D., H. M. Hurewitz, M.D., and Fred M. Smith, M.D., Iowa City, Iowa.

ABSTRACT

In perfusion experiments on the isolated heart of the rabbit theophyllin ethylenediamin produced a far greater and more consistent increase in the rate of coronary flow than did any of the various drugs tested. This drug was put to a more decisive test by observing its effect on the infarct produced by the ligation of a coronary artery in the dog. Observations were made during the initial stage of the infarction and after an interval of three weeks. In the first series of experiments a coronary vessel was ligated, and after the appearance of the distal area of cyanosis the drug was administered intravenously. This was followed by a decided reduction in the extent and degree of cyanosis, and in certain instances resulted in almost complete restoration of the original color. The drug was then given at daily intervals to a series of animals after the ligation of a coronary artery. These animals were sacrificed after an interval of three weeks, which, in view of the findings, allowed ample time for the restoration of the circulation to the area of infarction. This area was greatly diminished in these animals as compared to that in the control series which did not receive medication and in which a corresponding vessel was ligated at the same level. These results indicate that theophyllin ethylenediamin promotes the development of an extensive collateral circulation.

Discussion

Discussion of the papers on "Pathology of Coronary Sclerosis" and "Coronary Spasm as a Possible Factor in Producing Sudden Death" by Dr. Leary.

Dr. James B. Herrick, Chicago, Ill.—We are to be congratulated on having the opportunity of listening to these stimulating papers. The one pathological condition which is commonly found in coronary thrombosis is sclerosis of the coronary artery. Dr. Leary is trying to tell us what is the cause of this sclerosis and what is its nature. Possibly he can some day tell us how we may prevent it.

His work has at least an indirect bearing on the question of the frequency, or the possible increased frequency, of coronary thrombosis. The question is asked many times, "Is this disease increasing in frequency?" We know that, because more people are living to the coronary age, more cases are seen than formerly. Personally I believe that the special reason why the disease is increasing in frequency, or seems to be, is because it is today recognized by the clinician and by the pathologist. A few years ago it was overlooked by both. At any rate in looking over the literature one finds as far back as the time of Jenner and Parry that numerous cases of coronary thrombosis are down in the records as angina. Just the other day Dr. Levy and his coworkers showed that since the disease was recognized clinically, statistics reveal a sharp increase in the number of cases reported by the clinician and the pathologist.

I hope that Dr. Leary, later perhaps, can tell us what is the real cause of thrombosis, and its relation to the seeming increase in the disease. Statistics from

Germany and from other countries are by no means convincing that thrombosis has increased enormously. Some of the German writers are correct when they say that we must have better and more uniform standards of comparison than we have today with longer periods of observation before we can say to what extent thrombosis has increased.

One other point, and that is with regard to the sudden onset of coronary thrombosis. I am not referring to the cases of so-called gradual or chronic obstruction. Clinicians have been led to consider coronary thrombosis as nearly always a very acute incident. The explanation that Dr. Leary gives, the rupture of an atheromatous abscess, helps to explain why many cases are acute. But clinicians—perhaps the pathologists can explain why—certainly see some cases that they call acute where not for minutes, but for many hours, there are prodromal symptoms preceding the major outbreak. If an atheromatous abscess ruptures into the coronary, as I understand Dr. Leary, this really makes a plug at the point of narrowing. Is that always associated with an acute clinical manifestation? Are there cases in which the débris spills out into the lumen more gradually? Is this débris at times so thin, so fine, that it may be distributed distally, causing thus, as it lodges in the finer twigs, a disseminated thrombosis with patchy fibrosis as an ultimate result?

Dr. Leary referred to a fact about which I was going to speak, that there are cases in which a break in the wall of the vessel is followed by the entrance of blood into the wall of the vessel, really a dissecting aneurysm. My attention was first called to this occurrence by Dr. Gideon Wells of Chicago who said that he had noticed it in several cases. Dr. Moody of San Francisco showed me specimens that illustrated it. I recall also that Hyman and Parsonnet described a case. Is such dissecting aneurysm frequent?

This work is of such fundamental importance and has so many possible far-reaching bearings that it should be continued by Dr. Leary and confirmed by other investigators before being accepted in all its details.

Dr. Emanuel Libman, New York, N. Y.—I am not at all sure that rupture of atheromatous pockets will always lead to thrombosis, because one may encounter very extensive superficial areas of atheroma without any thrombosis supervening. I have drawn attention to the probability that there is an individual tendency to thrombosis (thrombophilia), and Dr. Herrick has just referred to the same subject. Thrombosis may occur in a vessel that is not much altered. On the other hand, extensive atheroma may occur throughout the aorta, without a trace of thrombosis. In another case of the same kind, there may be a thrombotic deposit in practically all the lesions. We know that atheromatous material may be discharged into the circulation, and occasionally one comes upon embolic lesions (skin) due to it.

While I believe that spasm occurs in the coronary arteries, it is difficult to secure post-mortem proof. It is possible that with careful studies, evidence may be obtained. I say this from an analogous finding. Many years ago, in a case of lead intoxication—fatal, due to intestinal obstruction—I found the last 18 inches of the ileum tightly contracted, although the examination was not made until several hours after death.

I would like to come back to Dr. Leary's main thesis, namely, the diathetic and metabolic aspects of coronary artery disease. For example, there is in some individuals a tendency to lay down connective tissue. This subject will now be more widely discussed because of the recent remarkable studies of Doljanski. In the course of studies in tissue culture, he was able to develop fibrillar tissue in plasma, with the aid of cellular products and in the absence of the cells themselves.

Furthermore, there is an individual tendency toward calcification. With regard to the subject of cholesterolemia and cholesterol deposition, I believe that a hepatic disturbance is primary. For some time I have held the opinion that in the con-

ditions which are commonly called "gouty" the disorder is largely connected with a disturbance in lipoid metabolism.

I should like finally to say a word in connection with the increasing frequency of coronary thrombosis. I believe that you will all agree that we now see fewer people in the street than formerly, who show the results of a cerebral thrombosis. It is possible that a number of those who formerly died of cerebral thrombosis at a late age, now die of coronary thrombosis earlier in life.

Dr. R. W. Scott, Cleveland, Ohio.—I should like to bring up for consideration here the younger group of patients that Dr. Leary mentioned whose coronary disease was characterized by fibrosis. I have been interested in such cases because of the obscure picture from an etiological standpoint which they present clinically. The ordinary signs and symptoms which aid us in establishing an etiological diagnosis are often absent. The patient runs a progressive downhill course, often extending over a period of several months. Advanced congestive failure is usually present at the time of death, and, as a rule, the diagnosis of coronary disease and myocardial fibrosis can be made only by exclusion.

I wonder whether Dr. Leary has any ideas as to the capricious distribution of the arteriosclerotic process in the aorta and the coronary arteries. Why is it, for example, that individuals who live seventy years or more have at autopsy no disease in the first two inches of the aorta? Why is it that the arteriosclerotic process may be sharply localized in a small area of the coronary artery and the remainder of the vessel show little or no involvement?

Dr. Edward B. Krumbhaar, Philadelphia, Pa.—While of course agreeing with Dr. Herriek as to the interest and stimulus attached to this point of view and to the evidence presented, I want to insert a word of caution, which doubtless Dr. Leary would agree with, that we should not on this account remove milk and eggs from the dietary! In the first place, results of metabolic studies on herbivorous animals such as rabbits must be transferred to man with great caution. Also there would have to be a correlation demonstrated between a high cholesterol intake and these lesions or at least some objective evidence of disordered cholesterol metabolism.

Dr. Walter W. Hamburger, Chicago, Ill.—I should like to ask Dr. Leary whether at autopsy he found similar changes in other vessels throughout the body. For example, in the renal artery or in vessels of the stomach and the spleen, whether changes in young and old individuals occurred in these vessels similar to changes in the coronaries.

Dr. J. P. Anderson, Cleveland, Ohio.—I should like to ask one question about the lipoid cells—Do they represent a fixed or wandering type of cell, i.e., are they endothelial cells engorged with lipoid material, or do they represent a fixed connective tissue type of cell in the arterial wall that imbibes the lipoid?

Dr. Harold E. B. Pardee, New York, N. Y.—I wish to ask Dr. Leary whether it is not difficult to distinguish between the grooving of the wall which he believes due to spasm, and such grooving as might result if the inner layers of the arterial wall were swollen and increased in volume, so that the circumference of the inner layers would be greater than the circumference of the outer layers.

Dr. Timothy Leary.—With reference to the frequency of acute thrombotic processes in coronary arteries it should be kept in mind that the material I have to deal with is derived from sudden deaths, occurring usually with little or no warning, and without medical attendance. My statistics show a definite increase in the numbers of this type of case. I am satisfied that the hard winter we went through had an influence in bringing to a termination many cases of coronary disease. I have certified

as many as six deaths of coronary type in one day this spring. The only symptom in most cases had been indigestion, which is more significant than angina in relation to sudden death. The character of the lesions found leaves no doubt as to the acuteness of the thrombosis. Coronary infarction is exceptional in this series.

Dissecting aneurysms of the coronary are rare in the literature and in my experience.

We recognize that the contents of an atheromatous abscess of the aorta are usually diffused without symptoms as far as they are recognizable. The delivery of a mass of semisolid mushlike material into a narrowed coronary artery, in my experience, tends to clog the artery locally, and is the standard cause of death in older persons. That this obstruction of the lumen by the contents of an atheromatous "abscess" is not an artefact is indicated by the occurrence of thrombi mixed with the contents of the atheromatous pocket in a high percentage of the cases. It is difficult to diffuse these contents through fluid blood, since they do not mix readily. It is impossible to diffuse the contents through clotted blood by any procedure which might be carried out post mortem. The influence of spasm in forcing the contents out of the atheromatous "abscesses" is suggested by the finding of the contents in the lumen and the cavity from which they came relatively empty and containing little blood. Rupture in the other direction, from the lumen into the "abscess," is found occasionally. The formation of clots on the site of ruptured atheromatous pockets in the aorta depends upon the area denuded of endothelium. If the "abscess" has ruptured through a small opening, no clot is formed. If the rupture includes wide tearing of the intima, thrombosis occurs.

This work should not lead to too critical an attitude toward eggs and milk. Cholesterol is a necessary part of the diet, and is important particularly in the growing period. The problem is basically one of metabolism. All the cholesterol in all the arteries in a patient with advanced atherosclerosis would weigh ounces at most. When one considers the years required to produce this deposit, the daily increment must be small. Perhaps we shall be able later to find some indicator on which we can base an estimation of the ability of the individual to handle cholesterol. Measures of the mobilized blood cholesterol will not suffice.

In none of my cases was there indication of myocardial insufficiency preceding the death, other than indigestion or a tired feeling. In only one of the cases was there evidence of so-called chronic myocarditis.

The connective tissue lining the coronary which is thrown into folds is not swollen. It is redundant and has a certain rigidity, but the fact that it is thrown into folds is evidence of narrowing of the lumen of the vessel, due to muscular tonus or to contraction.

We have no evidence as yet to offer with reference to the degree of atherosclerosis in other vessels.

It is my belief that the lipoid cells arise from the subendothelial connective tissue, though others believe them to be monocytes from the blood.

The work here discussed is presented not as a completed study, but as a report of progress. The Committee on Scientific Research of the American Medical Association has extended to me a further grant in aid for prosecution of added work. I shall be grateful for criticism in any or all phases of the subject.

Discussion of paper on "Coronary Arteriosclerosis, Coronary Thrombosis and the Resulting Myocardial Changes" by Drs. Saphir, Priest, Hamburger and Katz.

Dr. Edward Krumbhaar, Philadelphia, Pa.—I should like to speak of some relevant studies made by Dr. Polanco in our pathological department, where the amount of coronary sclerosis was observed in the various branches and correlated with the item of cardiac pain. Two hundred and thirty-six cases were analyzed in which

coronary disease was sufficient to be mentioned in the anatomical diagnosis. Sixty per cent of these, in our opinion, were really marked coronary sclerosis, and yet there were only thirty-four that showed any evidence of cardiac pain, and only ten showed old or recent coronary occlusion. Of these ten, only six had a history of cardiac pain. We did think, however, that we saw just what Dr. Saphir has emphasized, namely, that where there was coronary occlusion, sometimes it was multiple and sometimes the size of the infarct was undoubtedly influenced by a neighboring marked sclerosis, if not total occlusion.

We also studied sections from forty-four patients in six different parts of the heart and also in different organs of the body. We found that in all tissues examined there was some sclerosis, but the amount of sclerosis differed greatly. The heart, kidney, and spleen showed the most of any organs; in the others, it was almost negligible from the functional point of view. The same sort of thing was found in the six different parts of the heart. The descending branch of the left coronary was much more sclerosed than the others. Strange to say, the posterior descending was much less sclerosed than either of the circumflexes and was sclerosed to about the same degree as the two marginal arteries. Such findings merely emphasize again the patchy nature of the arteriosclerotic process and the need, if one is going to make an adequate study, of a very careful examination of all parts of the heart and the coronary distribution.

Dr. Emanuel Libman, New York, N. Y.—It is very interesting that Dr. Saphir and his colleagues found that in all their cases of infarction, two vessels were closed. I should like to know whether they feel that it is essential for infarction that branches of both the left and the right coronary arteries be blocked. According to my experience, this does hold true for infarction of the left posterior papillary muscle. This structure is supplied by the descending branches of both coronary arteries, and infarction occurs only when both are involved.

As regards the instances of infarction without closure of any large branch, the explanation lies partly in cumulative closure of small vessels. Apart from this, one must consider the question of spasm, and the possibility of toxic edema and toxic necrosis. Some years ago I observed a patient, suffering from subacute intestinal obstruction due to a carcinoma of the cecum, who developed a loud systolic murmur to the left of the sternum, which proved to be due to a perforation of the septum, secondary to necrosis. The heart showed a number of areas of necrosis, without any disease of the vessels to explain them.

Related to the studies of Dr. Saphir and his associates are some observations that I have made relating to the occurrence of jaundice in cases of coronary artery thrombosis, when not dependent upon another cause. In the cases that I have seen, few in number, there was present an old closure on the right side, and a recent one on the left. The explanation that has occurred to me is as follows: The closure on the right side leads to a disturbance of liver function. When occlusion of a large vessel on the left side then takes place, the collateral supporting the right side of the heart is much cut down, and there results a sudden increase in hepatic insufficiency. In organic disease of the tricuspid valve, jaundice not uncommonly supervenes, but it takes a long time—many years—for it to come. In these coronary cases it comes quickly, and therefore a remarkable opportunity is afforded for a study of acute hepatic insufficiency. I should like to know whether Dr. Saphir and his coworkers have had any experience with this subject.

Dr. Hamburger reported a number of years ago a case of jaundice associated with coronary thrombosis. I do not know whether a post-mortem examination was performed.

[Dr. Hamburger answered—No.]

Dr. Otto Saphir.—Dr. Priest a little later will discuss the relation of coronary thrombosis to pain as found in our thirty-four patients. I may say now that there was no relation at all between coronary thrombosis, severe coronary sclerosis and myocardial changes on the one hand to pain on the other hand.

In none of the hearts was there an infarct as the result of the occlusion of one branch of the coronary artery. Necrosis or infarction of the posterior papillary muscle was not encountered in this series.

The sclerotic process often extended into the smaller branches of the coronary artery. The arterioles, however, in none of these instances were diseased. As far as our experience goes, I might state that arteriosclerosis of the coronary artery is rare.

None of the patients with coronary thrombosis revealed jaundice.

Discussion of paper on "A Clinical and Pathological Study of Coronary Sclerosis" by Drs. Elliott, Evans, and Nuzum.

Dr. Robert L. Levy, New York, N. Y.—Dr. Nuzum said that there were certain cases which showed *practically* no coronary sclerosis. It is very difficult to determine, on a quantitative basis, just what degree of coronary sclerosis is functionally significant. Sometimes, what appear to be minimal lesions may be of great clinical importance. In the presentation which will be given later in the day by Dr. Turner, Dr. Bruenn, and myself, this fact will be stressed particularly in relation to pain.

Discussion of paper on "The Relation of Coronary Arteriosclerosis to Auricular Fibrillation With Special Reference to the Term 'Arteriosclerotic Heart Disease'" by Drs. Brown and Levine.

Dr. Wallace M. Yater, Washington, D. C.—I was surprised to see that this was the only paper on the program which had to deal with the arrhythmias relative to coronary sclerosis. Some years ago I made a study similar to this very interesting one of Drs. Brown and Levine on the pathological changes in cases of auricular fibrillation. Of 145 patients who came to necropsy there were only two hearts which had any great degree of coronary sclerosis, and both of these patients had shown hypertension clinically during life. I was forced to the conclusion that coronary sclerosis per se was a very rare cause of auricular fibrillation. There are, however, some arrhythmias, or better conduction disturbances which are definitely due, quite frequently, I believe, to coronary sclerosis. I refer particularly to auriculoventricular heart-block and bundle-branch block.

In a study of the conduction system by serial sections in cases of this kind. Cornell and I were struck by three things which I believe are relatively new: first, that A-V heart-block is not infrequently due to isolated lesions of the bundle branches, secondary to coronary sclerosis either of the large arteries or of the small ones; second, that it is extremely rare to find that only one bundle branch is involved by fibrotic changes and not the other; third, that the bundle branches may be extensively involved without any apparent pathological changes in the myocardium. It would seem, therefore, that the conduction system is more susceptible to a diminution of vascularity than the myocardium and shows changes sooner. We were unable to confirm the newer classification of bundle-branch block because of the great paucity of cases which have lesions confined to one bundle branch. This fact has been noted also by other workers.

I think the time has come when we need more studies by means of serial sections through the conduction system, because I believe we are drawing too many anatomical conclusions from electrocardiographic studies.

Dr. Louis F. Bishop, New York, N. Y.—I have been much interested in Dr. Levine's paper because we have made a recent study of so-called arteriosclerotic auricular fibrillation from the clinical standpoint. Dr. Levine stated that 80 per cent of the patients who came to necropsy had had hypertension. We found in our study somewhere around 50 per cent had hypertension, but a large number of these were women.

Dr. John J. Finigan, Rochester, N. Y.—I should like to ask Dr. Levine just one question. Just what age group did these fifteen patients with fibrillation fall into? Did they belong to the older age groups of sixty and seventy years, or to the younger age groups?

Dr. Samuel A. Levine.—Naturally we did not analyze the incidence of other types of arrhythmia, being concerned entirely with auricular fibrillation.

I think Dr. Yater's point is an important one. Fibrillation in coronary artery disease is not common. The arrhythmias he speaks of are common in acute coronary thrombosis. There is a great difference between proper and improper treatment of complete heart-block in acute coronary thrombosis. It may mean the difference between life and death. It is one of the few complications, I believe, in which the physician can function in a very important sense.

Dr. Bishop spoke about an incidence of 50 per cent of hypertension in his cases. I think our figure is a little greater because we included among those having hypertension those who had normal pressures at the time, but who were known to have had previous hypertension or well-marked changes in the retinal arteries, indicating a previous hypertension. The females are more hypertensive than the males in all cardiovascular diseases, and particularly in coronary artery disease—decidedly so.

We did not even think about the relation of possible chest injury to these cases. Dr. Finigan asked about the age groupings. I do not recall them accurately. We have them in our paper. I regret we did not regard it as important enough to indicate the exact ages. The fifteen patients with auricular fibrillation without heart disease included the five thyroid patients that we overlooked years ago (as I recall them, they were middle-aged people), six others with infections such as pneumonia, and four who had nothing to account for the fibrillation, who died of entirely unrelated conditions like leucemia or brain tumor.

Discussion of papers on "The Relation of Arteriosclerosis to Hypertrophy of the Heart" by Dr. Carr; and "Arteriosclerotic Heart Disease: Coronary Thrombosis and Its Effect on the Size of the Heart" by Drs. Horine and Weiss.

Dr. Ernst P. Boas, New York, N. Y.—I think it is the experience of most of us that in accordance with Dr. Weiss's study, a simple coronary occlusion is rarely ever followed by cardiac enlargement. I am under the impression, however, that, although a single coronary closure followed by survival for a number of years without heart failure is not followed by cardiac enlargement, in those patients who have multiple episodes of coronary closure, or who have slowly progressive subclinical closures with multiple myocardial infarcts, cardiac enlargement does occur.

I can recall two patients whom I have observed for a good many years, who had never had hypertension, and in whom cardiac enlargement occurred in the course of several years following multiple coronary episodes. It is my impression that the cardiac hypertrophy which always follows signs of cardiac insufficiency is in some way related to failure of the heart muscle.

Dr. Samuel A. Levine, Boston, Mass.—I should like to ask Dr. Weiss whether he has any information on the size of the heart temporarily. Is there some temporary dilatation?

Dr. W. R. Williams, Riverside, Ill.—I should like to ask Dr. Carr two questions. Does he find that adequate coronary circulation is essential for the development of the hypertrophy? In sclerosis of the coronary arteries, is this a late development in an already hypertrophied muscle?

Dr. James G. Carr.—The idea brought out in Dr. Williams' question occurred to us, but we have found no support for the view that a normal coronary circuit is more likely to be associated with cardiac hypertrophy than one with marked arteriosclerosis. It does appear that marked coronary sclerosis is frequent in connection with large hearts, especially in association with hypertension.

The most significant result of this study is the demonstration of many large hearts for which no cause can be assigned. Granting that the hypertrophy in many instances may have resulted from hypertension which had receded before the final illness, we are not justified in thus dismissing the entire group. In the presence of the data here presented, one may not deny the possibility that we are habitually overlooking causes of cardiac hypertrophy not now included in our categories.

In conclusion, attention should be directed to a few cases of a different type which are equally difficult to explain, namely, a few hearts weighing less than 325 grams which were associated with systolic blood pressures of 200 and above.

Dr. Morris M. Weiss.—We did not note at any time temporary dilatation of the heart immediately following the acute occlusion.

Those who state that coronary occlusion can cause cardiac enlargement do not mention the size of the heart at the time of the acute obstruction.

Clinical and pathological evidence of a preexistent hypertension should always be sought in any patient with an unexplained cardiac enlargement. As a result of coronary thrombosis a blood pressure previously high may fall to normal clinical limits and remain so for the remainder of the patient's life.

Our report did not discuss theoretical functional pathology. Some claim that from a functional point of view slow obliteration of coronary vessels must lead to cardiac enlargement. From analogy to vascular disease in other organs, coronary disease should theoretically result in atrophy of the heart.

Discussion of paper on "Arteriosclerotic Heart Disease in Diabetes" by Drs. Root and Sharkey.

Dr. Louis N. Katz, Chicago, Ill.—In some work carried out in collaboration with Drs. Soskin and Sol Strouse, we pointed out that when diabetes and heart disease are associated, the cardiac condition cannot be neglected in the therapeutic procedure for the diabetes. It was found unwise, in many such cases, to treat the diabetes too rigidly since the improvement in the diabetic manifestations was accompanied by a subjective and objective deterioration in the cardiovascular status. These patients reacted very favorably to a high carbohydrate diet, and it appeared that the blood sugar level consistent with well-being in such patients is higher than that which is considered desirable in diabetic patients without cardiovascular disease.

Dr. Samuel A. Levine, Boston, Mass.—There is a very important point involved in this topic in the relation between angina pectoris and diabetes. If diabetes is the causative factor and has something to do with the development of angina, treating diabetes rigidly will be a preventive in the life history of angina patients. I do not believe that this relationship has yet been proved.

It would seem to me that if diabetes were productive of angina pectoris in a causative sense, the patient who has diabetes ought to have angina earlier in life and die earlier in life than nondiabetic angina patients. Years ago the analysis we made of the nondiabetic and the diabetic patients with coronary thrombosis showed that they got the disease and died at about the same age. Dr. Root's figures today—63

years for hypertensive and 51 for nonhypertensive—are approximately the age of death from coronary artery disease in nondiabetic individuals. Are we not more justified in assuming that both conditions are manifestations of the same inherent defect or tendency? For example, if you took freckled children and nonfreckled children, you would find that more freckled than nonfreckled children have rheumatic heart disease. That is to say, the freckles may indicate a vulnerability to the disease. If we took two diabetic twins coming from parents with diabetes or vascular disease, one kept from developing diabetes by treatment and by prohibiting obesity, might it not be that we would find both to have coronary artery disease at the age of forty-eight or fifty-three years, the one a well-treated diabetic who had been prevented from becoming obese, the other definitely obese? Our figures on angina and obesity show the same thing; that obesity does not enhance the development of angina. May not obesity and diabetes be mere homologs indicating the same type of vulnerability?

Dr. Wallace M. Yater, Washington, D. C.—In the same connection as Dr. Levine's discussion, I wonder whether Dr. Root noticed a greater incidence of coronary sclerosis among the treated diabetic patients than among the untreated.

Dr. H. F. Root.—It is difficult to classify patients according to the degree of successful treatment and control of diabetes. A perfectly treated diabetic person is rare. Furthermore our standards of proper treatment have changed rapidly in the last fifteen years. We think some of our patients are well treated, but we do not know what happens to them a large part of the time. Everybody knows that diabetes in patients may be severe this year and next year may be mild; the year after that be severe again. The duration of the disease is one thing that you can be pretty definite about, and whether the patients are young or old, the duration is an important thing.

Modern treatment is better than the old treatment. I am sure more judicious use of insulin gives better results than in the past, and we are seeing fewer calcified arteries in the legs of children. Autopsy findings shed some light on the question of whether the vascular lesions are due to an inherited tendency or are secondary to the diabetes. Shields Warren examined a series of nearly 300 nondiabetic persons, and found as much arteriosclerosis in the pancreatic vessels as in the diabetic persons. Second, he examined nearly 300 diabetic individuals and found only 27 per cent had arteriosclerosis in the pancreatic vessels.

Dr. M. H. Nathanson, Minneapolis, Minn.—Several years ago I made a similar study on one hundred autopsied diabetic persons. I compared the incidence of coronary disease with a group of 250 nondiabetic persons. Fifty-two per cent of the diabetic patients above the age of fifty years showed extensive coronary disease as compared with an incidence in the same decades of 8 per cent for the nondiabetic group. Thus, the incidence of extensive coronary disease was six and one-half times greater in diabetic than in nondiabetic persons.

In the nondiabetic individuals the preponderance of males over females showing coronary disease was 3 to 1. In the diabetic series the ratio was 1.8 to 1. This indicates that the comparative immunity of the female to coronary disease is distinctly lessened when diabetes is present.

The mode of death was also studied. About one-half of the diabetic patients showing severe coronary disease died a cardiac death. Of these two-thirds died of congestive heart failure and in one-third the death was anginal in type.

The age incidence of diabetes is important. We know that 10 per cent of all the cases begin in childhood without arteriosclerosis. Forty per cent of them begin before the age of forty years. Diabetes disappears in old age. We now know that the peak of incidence in diabetic persons is between fifty and fifty-five years and per-

haps earlier. Then incidence falls, and at seventy a man is no more likely to develop diabetes than he was at twenty. This significant observation of Pincus and White is rather against the supposition that arteriosclerosis causes diabetes.

I am very grateful for the comments of Dr. Nathanson. The great frequency of coronary disease seems to me incontrovertible and the emphasis should be upon judicious treatment. The fact that extremes of chemical change in blood and tissues either in one direction or the other in the diabetic have a bad effect upon coronary disease, seems indicative of a metabolic influence.

Discussion of paper on "Valvular Atherosclerosis" by Drs. McGinn and White.

Dr. Emanuel Libman, New York, N. Y.—This important subject is now receiving some of the attention which it deserves. For a long time the calcific lesions of the heart, whether secondary to an inflammatory process (rheumatic fever, subacute bacterial endocarditis, etc.), or not, have been neglected. Because the term "Mönckeberg's sclerosis" is so much identified with the Mönckeberg calcification of the media of arteries, I believe it would be advantageous to designate the valvular lesion discussed by Drs. McGinn and White, "Mönckeberg valvular lesion," or still better, "annular fibrosis or sclerosis," and if calcification be present, "annular calcification" or "ring calcification."

There is a murmur which is often characteristic of calcification of the mitral ring, and by means of which one can at times suspect its presence, in persons over thirty-five to forty years of age. It is a systolic murmur heard best to the left of the sternum. It may be present along the left sternal margin up to the position of the pulmonary artery. The first sound is generally audible, merging directly into the systolic murmur which is likely to be rough, often whistling in character, at times musical. It is transmitted to the right as much as to the left, and is less loud at the apex. It is usually not heard beyond the apex. If there be present a similar murmur in the area of the aortic orifice, one must be cautious in venturing an opinion because the parasternal murmur may be only a transmitted one.

This subject is very important, because in rheumatic fever there is often heard a murmur in the same position, especially early in the disease. It is likely to be somewhat rough in character, not smooth like the early murmur of insufficiency, which is loudest at the apex and markedly transmitted to the left. Because of my experience with the murmur due to ring calcification (and ring sclerosis?) I have for a long time suspected that the murmur heard best in the same location in rheumatic fever may be due to valvulitis of the mitral ring (perhaps at times, valvulitis of the pulmonary artery). This murmur not infrequently disappears when a mitral insufficiency develops, resulting from sclerotic changes at the free border of the valve. In cases of rheumatic fever it is important to listen carefully at the left border of the sternum, as well as at the apex and base of the heart.

Sibson knew of this early murmur in rheumatic heart disease, and described it with great care. He interpreted it as being due to relative tricuspid insufficiency. This explanation cannot be correct, because if it were, the murmur should become louder when a real mitral insufficiency develops. Like some other observers, however, Sibson himself noted that the murmur often disappears as a mitral insufficiency develops.

Dr. McGinn.—It is true, we generally think of Mönckeberg's sclerosis as medial sclerosis of the medium-sized peripheral arteries. Mönckeberg has also described a distinct atheromatous and sclerotic change involving the base of the aortic cusps and in this same paper has given a remarkably clear description of the histology of the aortic valve cusps. To retain the name of Mönckeberg's sclerosis of the aortic valve for these lesions would direct attention to his valuable observations. A similar process

may, however, involve the mitral valve so that the term "annular sclerosis" may well include such lesions of the aortic and the mitral valve under one terminology and is probably preferable to Mönckeberg's sclerosis.

Discussion of paper on "Coronary Arteriosclerosis, Coronary Thrombosis, and the Resulting Myocardial Changes" by Drs. Priest, Hamburger, Katz, and Saphir.

Dr. Morris M. Weiss, Louisville, Ky.—Some racial and social observations on pain in coronary artery disease may be of interest. A history of classical angina pectoris is uncommon in the Louisville City Hospital patients with coronary disease, whereas it is a frequent complaint in our private cases. It is especially rare in negroes, although they have coronary disease with a frequency equal to that in the white race. We believe this is due to the lack of intelligence of the average city hospital patient, especially the negro, who is unable properly to interpret and describe his symptoms.

Pain lasting a half hour or more or a marked fall in blood pressure are considered pathognomonic of a coronary occlusion. This has not always been our experience. Attacks of angina pectoris may last up to two hours without subsequent clinical evidence of coronary thrombosis. Also the blood pressure may temporarily rise during a coronary occlusion.

Dr. Walter S. Priest.—I am glad Dr. Weiss emphasized the points that he did. From the results of this study, I know some of us have become reluctant to make a positive diagnosis of coronary thrombosis or myocardial infarction in any given case.

Dr. Weiss emphasized the pain feature and the blood pressure feature. Again referring to the patient whose slide I showed; when one can see a patient have an attack of pain lasting as long as four hours and associated with the other characteristic clinical symptoms and yet not have a coronary thrombosis or myocardial infarction, it makes one wonder whether many of these attacks which we have diagnosed clinically as undoubted coronary thrombosis should have been so diagnosed.

Discussion of papers on "Significance of the Coronary Circulation in Arteriosclerotic Heart Disease" by Drs. Smith, Paul, and Rathe; and "Mechanism of Pain Production in Angina Pectoris" by Dr. Katz.

Dr. Joseph B. Wolfe, Philadelphia, Pa.—The paper presented by Dr. Katz and the one by Dr. Smith are extremely important from a clinical point of view. They tried to show that one must keep in mind other factors, not only coronary disease as the causative factor in precipitating the painful syndrome of angina pectoris.

Dr. Katz presented experimental evidence to support the theory that angina pectoris may be of neurogenic origin. It has been shown that many nociceptors like an abnormally functioning thyroid, gallbladder, psychic and metabolic disturbance may be responsible for the syndrome of angina pectoris.

I have already called attention to the possibility not only that angina pectoris is frequently of neurogenic origin, but that coronary T-waves may be caused by neurogenic disturbances. I have shown that pancreatic extract apparently due to its lecithinogenic property and its influence upon muscle metabolites, tends to relieve angina pectoris and intermittent claudication.

This points to the possibility that metabolic, particularly lecithinogenic, dysfunction, may be another factor in the causation of angina pectoris. Dr. Smith stresses coronary disease as an etiological factor in angina pectoris, and Dr. Katz calls attention to the possible neurogenic elements in angina pectoris. We therefore should still keep an open mind as to the many possible causes of this symptom complex.

Dr. Walter W. Hamburger, Chicago, Ill.—I should like to ask Dr. Smith this question: Was the paroxysmal dyspnea usually nocturnal in origin, and if so does not Dr. Smith feel that paroxysmal dyspnea is usually a sign of left heart failure, as Paul White and others have declared? And if he does feel that paroxysmal dyspnea is a sign of left heart failure, does he believe that such attacks always mean occlusive changes in the coronaries, particularly in the left side of the heart?

Dr. Walter S. Priest, Chicago, Ill.—In connection with Dr. Smith's mention of the development of angina of effort following coronary occlusion, I might state that in the group I reported this morning 30 per cent of the patients who had angina of effort developed the angina of effort following coronary occlusion or myocardial infarction.

Dr. Andrews.—Some time ago I had the opportunity to observe a patient who had a phlebitis migrans in which at one time or another most of the vessels throughout the body were thrombosed. At one period in her course, she had some precordial distress, and the electrocardiogram became abnormal. It was my impression at that time that she had thrombosis of some of the coronary veins. The significance of it did not impress me at that time, but I have wondered many times since whether that did not involve a disturbance in the carrying away of the various waste products and gave close to an anginal syndrome.

Dr. Katz's observation here in regard to the compression of the coronary arteries and veins has been very interesting to me.

Dr. Harold E. B. Pardee, New York, N. Y.—I, too, have seen a case very similar to the one just mentioned in which phlebitis migrans was followed by a typical clinical picture of coronary occlusion with electrocardiographic changes. It seems quite evident that this picture may result from venous as well as from arterial disease.

I wish also to emphasize one of the things which appeared in Dr. Smith's paper, that is, the great frequency of the syndrome of cardiac insufficiency. The development of this syndrome is a well-recognized result of coronary arteriosclerosis, but it happens that the present fashion of diagnosis and treatment has led us to talk very much more about the anginal syndrome. I noticed that in Dr. Smith's series the cardiac insufficiency syndrome was the most frequent clinical picture.

Dr. Oille, Toronto, Ont.—We also had a patient with phlebitis migrans who developed symptoms and electrocardiographic findings of coronary occlusion. Thrombosis in the coronary sinus was diagnosed and proved at autopsy.

I should like to emphasize Dr. Pardee's last remark and stress the point that dyspnea is a common and perhaps a more important manifestation of coronary disease than pain. Dr. Rykert and I have recently analyzed the last ninety cases of severe coronary disease that came to autopsy in the Toronto General Hospital. Of these, the largest group was characterized by dyspnea and congestive failure. In addition, dyspnea appeared to be a more serious symptom than angina, because, in the patients whose first symptom was angina, the duration of life averaged forty months. In those patients whose first symptom was dyspnea, the average length of life was twenty-eight months. The duration of life after nocturnal dyspnea commenced was eleven months. These figures, of course, are not averages for all cases of coronary disease, but merely represent the average length of life of this serious group of ninety individuals.

Dr. Laplace, Philadelphia, Pa.—I should like to call attention to a further analogy between angina pectoris and experimental muscular ischemia as described by Dr. Katz. Dr. Martin Crane and I have performed similar experiments on a

series of hospital patients and found that many subjects developed muscular fatigue which terminated the exercise before the appearance of severe pain. We concluded that an explanation of the absence of pain in many cases of myocardial ischemia might be found in the possibility that in such cases fatigue may prevent the cardiac muscle from working to the point of pain production. Our experiments were originally designed as a quantitative test for sensitivity to the pain of muscular ischemia. We found that no abnormal sensitivity of this type could be demonstrated in patients with angina pectoris, and we concluded that nervous hypersensitivity is therefore unlikely to be an important factor in determining the occurrence or degree of pain resulting from myocardial ischemia.

Dr. Fred M. Smith, Iowa City, Iowa.—Paroxysmal dyspnea is commonly indicative of a left ventricular failure. We wished to emphasize the importance of bearing in mind the possibility of coronary occlusion, especially with the first attack and particularly in those who heretofore have been free from cardiac symptoms. The paroxysmal dyspnea frequently occurs at night, but in several instances of our series first appeared during the day following exertion.

We were impressed with the high incidence of congestive failure as the initial manifestation of cardiac disease in our series of cases. It was felt that in certain instances the congestive failure followed an unrecognized coronary occlusion. The prognosis was in general graver in this group of patients. There was little time to speak of electrocardiographic findings, but you may be interested in knowing that 30 per cent of those beginning with congestive failure had bundle-branch block. The incidence of this finding was highest in this particular group.

Dr. Louis N. Katz, Chicago.—We found two factors primarily concerned with the production of pain. The first is ischemia, and the second is the state of the nerve apparatus. Our work has led us to conclude that ischemia produces a chemical substance, diffusible in character and probably acid in nature, which acts as a stimulus for pain production. Our work has shown that the pain produced by occlusion of the coronary vessels in the dog is due to irritation of the sensory nerve fibers and not to occlusion of the artery itself.

Our experiments further show that these pain fibers are confined to the region of the coronary vessels. Pain responses were not obtained when other regions of the myocardium were compressed. Woollard has shown that these sensory fibers congregate around the mouths of the coronary vessels. It is conceivable that the involvement of these fibers by syphilis at the root of the aorta might explain the anginal attack, without invoking actual occlusion of the mouths of the coronary vessels. Similarly the blind manipulation involved in probing the mouths of the coronary arteries, such as carried out by Sutton and Lueth, might easily give rise to pain by stimulation of the nerve plexus surrounding the coronary mouths and not, as they assume, by closing off the coronary blood supply. Even sudden death preceded by agonal struggle might be due to ventricular fibrillation, the direct or reflex result of stimulation of this plexus.

We have obtained evidence that fatigue is a variable which modifies the pain response from skeletal muscle. We have found in our work that fatigue is a disturbing element. The subject, as first pointed out by Laplace, may, on occasion, stop contraction because of fatigue and not unbearable pain. In one subject we found that, following a short period of bodily exercise, the subject was unable to contract the muscles after his arm was made ischemic because of fatigue. It may be that the element of fatigue determines whether signs of congestive failure or anginal attacks occur in coronary sclerosis. This concept, however, demands further proof.

Discussion of Symposium on Electrocardiogram Phases of Coronary Arteriosclerosis.

Dr. Louis N. Katz, Chicago, Ill.—There are a number of things that might be discussed but the limitation of time will permit me to take up only one or two. The concept presented by Hiss and Robb that the contour of the electrocardiographic distortion is determined by the bundle of muscle involved is very interesting and may be the ultimate solution of our inability to locate infarcts accurately with ordinary leads. The result of work done in our laboratory indicates that the electrical currents are conducted away primarily by the posterior muscle mass. It might well be that the conduction of electric currents may be best along the muscle bundles, and so the electrocardiogram will depend on the location of the muscle bundles to the posterior muscle mass.

The plea of Dr. Barnes to utilize the ordinary leads more than we are before introducing any other leads cannot pass unchallenged. I think there is today a temptation to read into the standard leads significance based on very minor changes which might easily be subject to personal interpretation. This tendency makes the reading of electrocardiograms a mysterious process to the average physician. From a personal experience with an extensive series of electrocardiograms I am convinced that the electrocardiogram is very valuable in the interpretation of coronary disease. The use of chest leads has been a valuable addition. While I do not advocate the use of nine leads for ordinary purposes, I feel, from the experience of Wilson, of Wolferth and Wood and at our Heart Station, that many cases of recent coronary occlusion would be missed if a fourth (chest) lead were not taken. We feel that the position of the anterior electrode is important: the posterior one can be placed practically at will. While the ordinary three leads have not been very useful in our hands in locating infarcts, the fourth lead has so far been infallible in our autopsy cases. It would be a pity to discourage the wide use of a fourth (chest) lead, particularly in suspected cases of recent coronary occlusion.

Dr. Samuel Bellet, Philadelphia, Pa.—I should like to mention some of the work we have been doing with precordial leads in conjunction with Drs. Wolferth, Wood and McMillan. At the present time we have a total of 104 cases of coronary occlusion which we have studied by both the indirect and the precordial leads; 22 of these cases have been studied at necropsy. In 40 per cent of these cases, we were able to make a diagnosis by the precordial leads, whereas the indirect lead at one time or another did not clearly indicate such a diagnosis. In addition to the value of the precordial leads in the diagnosis of coronary occlusion, the progression of the lesion can be followed better by the direct chest leads than by any other means at our disposal. This is true chiefly in cases of anterior occlusion. The state of the lesion can be predicted by the configuration of the S-T interval and the T-wave in the precordial leads. These changes may be present for two to three weeks, sometimes for several months, during which time alterations in the T-waves of the indirect leads may or may not be observed.

The precordial leads are also of help in the diagnosis of old anterior infarctions. In the indirect leads the T-waves inverted in Lead I following an anterior occlusion often become upright in the chronic stage. The electrocardiographic diagnosis of such coronary occlusion is impossible from such a tracing as shown in the slide presented by the last speaker. However, examination by precordial leads in the case of anterior occlusion frequently discloses the presence of an old infarction. This is shown by the absence of the initial downward deflection in Lead IV, with no S-T interval deviation. We have had under observation three patients with old coronary occlusions showing the signs just mentioned. In two cases, post-mortem examinations have confirmed the diagnosis; in the other case, the history of a previous

coronary occlusion is quite clear. Many others of our cases followed to the chronic stage, showed similar changes.

The differential diagnosis between the electrocardiographic evidence of acute pericarditis and that of coronary occlusion should ordinarily not be difficult. We have recently had two such cases. The S-T intervals are elevated in all three leads in acute pericarditis, a condition which does not occur in simple coronary occlusion. The differentiation from anterior coronary occlusion is aided by the use of precordial leads which show the maintenance of the initial downward deflection, and the S-T interval situated below the isoelectric line.

Dr. William J. Kerr, San Francisco, Calif.—It seems to me that the paper presented by Dr. Hiss is one of the most important we have heard in some time. I should like to question Dr. Robb concerning the penetrating branches of the coronary vessels. In our experience the penetrating vessels of the ventricles run perpendicular to the superficial branches and supply the muscle clear through to the intima. I should like to ask Dr. Hiss whether his studies suggest that the penetrating branches supply the entire wall. Does occlusion of the vessel at some point near the base cause a selective damage to a certain layer of muscle? If so I cannot understand the function of the penetrating vessels unless they give off collateral branches between layers.

Dr. Jane Sands Robb.—If I may answer a question in regard to these penetrating branches, the superficial muscles obtain their blood supply from certain of the longer branches as they run on the surface of the muscle or between the first and the second layer. There are other branches which are short and give off no superficial branches, but penetrate to the deeper muscles, so that by choosing the branches which one ligates, one can get a lesion in a deep muscle without involving the superficial circulation.

Dr. A. R. Barnes.—I should like to correct an impression that I am against taking direct anteroposterior chest leads. We have taken them on about 2,500 of our patients. I do want to stress the fact that we should not lose sight of the old tools that have served us in good stead and that we should not be carried away by our enthusiasm over the so-called fourth lead.

Dr. Howard B. Sprague.—I agree with Dr. Barnes and Dr. Katz in relation to chest leads. I think that we must use them because of the sort of information that I have reported this afternoon. However, we must decide on the simplest, most efficient method which is clinically practical. There are many reports of electrocardiographic studies using chest and other leads without autopsy control. Autopsy work leads to considerable humiliation, for it is sometimes very disappointing to find that the heart at necropsy does not support the finely spun theories and predictions of cardiac pathology made upon the basis of electrocardiographic study.

Discussion of paper on "Observations on Prognosis in Angina Pectoris" by Drs. Wedd and Smith.

Dr. Samuel A. Levine, Boston, Mass.—I have had similar results as to prognosis in angina pectoris. This last year we published a review similar to the one that Dr. Wedd has given us. We tried to get some clue to predict which patient is going to die in a week and which is going to live for twenty-five years. A few lived only a short time after I saw them, but the extreme was twenty-five years. Blood pressure level did not help; heart size, murmurs, electrocardiograms were a complete disappointment; in fact, we learned something unexpected from them, namely that those who had abnormal electrocardiograms had a longer life, a longer duration of angina, and a greater age at death than did those with normal curves.

There is one point to which I should like to differ, that is the factor of inheritance. We have, I believe, pretty definite evidence in our group that inheritance is important. In fact, the only clue we found is that angina patients who were born of long-lived parents lived longer than those born of short-lived parents.

Incidentally, we have some indirect evidence to show that we inherit the defect from our mothers rather than from our fathers; that is, the female is more responsible for handing down vascular vulnerability, although she suffers from angina a good deal less than does the male.

Discussion of paper on "Treatment of Various Forms of Arteriosclerotic Heart Disease by Means of Total Ablation of the Normal Thyroid Gland" by Drs. Blumgart, Riseman, Davis and Weinstein.

Dr. James Alexander Lyon, Washington, D. C.—I have listened with great interest to the paper by Dr. Blumgart and his associates. The total ablation of the thyroid gland is a major operation and, as has been stated, may be followed by myxedema. Dr. Edmund Horgan of Washington, D. C., and I have obtained very beneficial results in two cases of angina pectoris by performing a much simpler operation; that is, the division and ligation of both superior and both inferior thyroid arteries. As far as we know this operation has not previously been performed in the treatment of heart disease.

In studying a group of 300 patients, five to ten years after thyroideectomy, we made an observation which we considered important. We found that in the cases in the group which had been considered persistent hyperthyroidism, recurrent hyperthyroidism, and "thyrocardias," the patients were apparently free of symptoms. There was no evidence of hyperthyroidism, and no tachycardia or auricular fibrillation. These patients had been treated surgically by a method which included the division and ligation of both superior thyroid arteries and the ligation of both inferior thyroid arteries. We concluded from our observation that stopping the effects of hyperthyroidism in these patients was due to two things: first, the removal of the major portion of the thyroid gland; second, and chiefly, the division and ligation of the superior thyroid arteries and the ligation of the inferior thyroid arteries. This latter procedure cut the pathway of nerve stimuli from the sympathetic nervous system to the thyroid gland. As the results of the division and ligation of the superior and inferior thyroid arteries had been so beneficial in the patients referred to above, we considered cutting off the major portion of the blood supply and cutting the nerve pathways from the sympathetic nervous system to the thyroid gland in cases of angina pectoris and congestive heart failure by the division and ligation of both superior and both inferior thyroid arteries. We had an opportunity to perform this operation in two cases; one a patient with angina pectoris who had been observed over a period of five years prior to and five and a half months following operation; and one a patient with aortic regurgitation and angina pectoris who had been observed over a period of seven months prior to and two months following operation. We feel that the clinical improvement in these patients has been so remarkable that the cases should be mentioned here.

The division and ligation of all the vessels at the superior poles of the thyroid gland and the division and ligation of the inferior thyroid artery markedly reduce the blood supply and cut off the sympathetic nerve supply to the thyroid gland. The effect of cutting down the amount of blood entering the thyroid gland and cutting off all stimuli from the sympathetic nervous system is to decrease the basal metabolic rate, to reduce the circulatory demands, and to lessen the work of the heart. We have employed an operation much simpler than the total ablation of the thyroid gland as done by Drs. Blumgart and Berlin. We do not sacrifice a vital organ such as the thyroid or parathyroids. Myxedema is not produced but the basal

metabolic rate is lowered. By leaving the parathyroids undisturbed we do not cause an alteration of the calcium metabolism.

Dr. Samuel A. Levine, Boston, Mass.—We have had about 45 patients operated on by total thyroidectomy at the Brigham Hospital in the past year and a half. The results are similar to those presented by Dr. Riseman. I do not think they warrant quite the same degree of enthusiasm, and yet I have no doubt at all in my mind but that people who were refractory to the methods of treatment we were familiar with have been specifically helped by these procedures.

I think that no one should be operated on who can work without it, or who can be comfortable without the operation; so that very mild cases should not be selected, and those patients who are too sick also should not be selected. There is a group in between where choice can be exercised.

Although this concerns total thyroidectomy, one word might be said about partial thyroidectomy. In the case which made this study of thyroidectomy develop the patient was a woman who was operated on in 1927, who had a partial thyroidectomy done. I followed her for four years, and she had a most unexpected improvement. This was reported about two years ago and precipitated the work subsequently done on complete thyroidectomy.

Dr. Blumgart, after the experience of the first two or three cases we had very properly advised a total removal because a partial removal might be a failure, as the remaining gland could regrow. One of those partial cases, however, is about as good a result as we have had in our entire series. The first patient with partial thyroidectomy of this latter series has been working for about a year and a half. He developed myxedema, in spite of the fact that only a partial thyroidectomy was performed. He had not been able to work at all before, and he is comparatively free from attacks now.

Dr. Herrman L. Blumgart.—The question of subtotal thyroidectomy of the normal gland for the treatment of heart disease is a very interesting one and has been studied by various investigators in the past. Crile, Riesman, Boas and Shapiro, Dautreband, Rose, and others performed subtotal thyroidectomies in patients with no evidence of thyrotoxicosis evidently in the hope that just as this operation lowers the abnormally high rate of thyrotoxicosis to normal, so the normal metabolic rate would be reduced to a subnormal level. While this may occur occasionally, there is no evidence in the literature that subtotal thyroidectomy can be relied upon to produce a permanently subnormal metabolic rate. In the first two cases that engaged our interest, only transient relief was obtained by subtotal removal of the normal gland, the period of relief paralleling the curve of decline in the basal metabolic rate. After some weeks the metabolic rate returned to its preoperative level and the patients' condition relapsed to its previous status. In accord with Halsted's experimental work reported in 1907, we felt that the minute remaining fragments of normal thyroid tissue had undergone sufficient hypertrophy to sustain a normal metabolic rate.

Our earlier work on the circulation, particularly the velocity of blood flow, led us to believe that nothing short of a persistent hypothyroid state with its low metabolic rate would release the heart from its normal burden. Although maximal subtotal thyroidectomy was done in our first two cases, we failed in our primary purpose to reduce permanently the basal metabolic rate. Even if success might occasionally attend subtotal thyroidectomy, it became apparent that nothing but complete removal of every vestige of thyroid tissue would regularly insure a permanent subnormal metabolic rate and clinical improvement.

After success attended the first complete ablation of the thyroid (Case 3 of our first communication, Blumgart, Levine, Berlin: *Arch. Int. Med.*, June, 1933), a

subsequent attempt was made to remove the remaining fragments of tissue in Case 1, in which there had been a relapse to the preoperative clinical condition. Dense adhesions were encountered which made identification of thyroid fragments impossible. It was felt that any surgical dissection would be extremely dangerous because of the difficulty of identification and consequent likelihood of injury to the parathyroid glands or recurrent laryngeal nerves. Heavy dosages of roentgen radiation were employed but without effect.

Our observations (Friedman, H. F., and Blumgart, H. L.: J. A. M. A., Jan. 6, 1934) led to the conclusion that little could be expected from roentgen radiation as a substitute of surgery or an adjunct to subtotal thyroidectomy in the treatment of chronic disabling heart disease. In brief, the failure of others and of ourselves to benefit patients by subtotal thyroidectomy, our unsuccessful attempt to remove residual fragments at a subsequent operation, and the ineffectiveness of roentgen irradiation on the remaining tissue emphasize the therapeutic importance of removing the entire gland at the time of the first operation. Ample confirmation for this conclusion has been obtained by our subsequent experience in some seventy-five cases of angina pectoris or congestive failure, in all of which the hypothyroid state has persisted after total ablation of the thyroid gland, and in practically all the patients clinical improvement has occurred.

At the present time nothing but the complete removal of every vestige of visible thyroid tissue by surgical means will regularly insure the desired persistent hypothyroid state with its lowered metabolic rate and consequent clinical improvement. Recently, since the inception of our work, some investigators have performed maximal subtotal thyroidectomies, but the results have been disappointing, the metabolic rate has returned to normal, and the clinical condition has been unimproved.

Discussion of paper on "Theophyllin in the Treatment of Arteriosclerotic Heart Disease," by Drs. Smith, Paul, and Rathe.

Dr. Cooksey, Detroit, Mich.—Of interest in connection with Dr. Rathe's paper is an event which occurred in our cardiac clinic at Harper Hospital in Detroit. We have been faced with rigorous curtailment of the cost of drugs to patients of the Out-Patient Department. In treating angina of effort and related disturbances, we found it necessary to use something extremely inexpensive. A comparative study was made on a series of cases to determine whether theophyllin and all the closely related substances thereto were, after all, any more effective than some of the less expensive substances. The one to which we first, of course, turned, was the alkaloid of theobromine. As you probably know, it is very inexpensive.

We found that by the use of theobromine alkaloid, the effects in relieving angina pectoris and nocturnal dyspnea seemed just as good as they were in our private patients who were receiving metaphyllin and theocin. Also comparative studies were made on the same patients by the use of the various drugs with the same results. It has been our experience that theocin often produces nausea if given in very large amounts, so we do not often use it. Metaphyllin works extremely well.

Discussion of paper on "Tolerance to Digitalis in Patients With Normal Hearts and in Those With Arteriosclerotic Heart Disease," by Drs. McMillan, Bellet, and Robertson.

Dr. Samuel Bellet, Philadelphia, Pa.—The statement is often made that digitalis should be given until beneficial effects are obtained, or until the patient vomits. If this procedure is followed, many severe toxic reactions will occur.

In the normal group, 17 of our 20 patients vomited. They all received massive doses of the drug, and in spite of vomiting they showed no serious toxic effects.

In none of this group were extrasystoles, which we consider as definite evidence of toxicity, present even after the large doses administered. The group with slight myocardial disease reacted practically like the normal group. In the group with advanced myocardial disease only 9, or 40 per cent, of the patients, vomited. The remainder developed severe toxic reactions before vomiting occurred. These reactions, in 12 of this group, consisted of psychosis in two cases, severe visual disturbance in one, marked asthenia in three, and most important, the presence of toxic rhythms (ventricular tachycardia, complete A-V block, auricular tachycardia, nodal rhythm and bigeminal rhythm) in six patients. All these patients belonged to the arteriosclerotic group. In many of these patients, the toxic reactions were produced at comparatively small doses. We regard this point, namely that toxic digitalis manifestations may appear without the patient's vomiting, as extremely important. If this is kept in mind, many toxic reactions may be avoided.

In addition to the evidence which has been presented that a diminished tolerance to digitalis exists in patients with advanced heart disease, we should like to mention some evidence from the experimental standpoint. We took a series of normal dogs and standardized them with digitalis. We then produced cardiac damage in a series of these animals by tying the coronary arteries. These animals were standardized during the stage of acute, subacute, or chronic infarction. We found definitely diminished tolerance during the stages of subacute infarction, during which the infarcted area is at its maximum.

In conclusion, there are two points especially which we should like to make. First, patients with advanced myocardial disease exhibit a diminished tolerance to the digitalis as compared with a normal group. This diminished tolerance is, apparently, especially pronounced in the arteriosclerotic group. Second, toxic rhythms and other evidences of digitalis toxicity may be present without the patient's vomiting.

Department of Reviews and Abstracts

Selected Abstracts

Gordon, Wayne, and Adams, Wright: Estimation of Cardiac Transverse Diameter in Children and Comparison With Cardiac Area. *Am. J. M. Sc.* 188: 491, 1934.

The relations of cardiac area and cardiac transverse diameter as measured by the roentgen ray, to sitting height, height, weight and age have been studied in a group of normal children. Both measures correlate better in children with weight than with height or age.

An equation is presented for the prediction of normal transverse diameter, and a comparison is made with cardiac area prediction formulas previously published from the same material.

Cardiac area in normal children can be predicted with greater accuracy than transverse diameter by any of the measures used. The advantage of cardiac area over transverse diameter as a measure of normal heart size appears to be greater in children than in adults.

Roesler, H.: Interatrial Septal Defect. *Arch. Int. Med.* 54: 339, 1934.

A case is reported which illustrates the clinical and anatomic peculiarities of interatrial septal defects. Sixty-two cases have been reviewed. All of the cases of small defects or complete absence of the interatrial septum and combinations with patency of the ductus arteriosus, pulmonary stenosis, interventricular septal defect, and a high grade of coarctation of the aorta have been excluded.

In at least three-fourths of all the cases, valvular lesions were found which affected predominantly the mitral orifice. Subacute bacterial endocarditis did not occur; chronic pericardial disease, crossed embolism and tuberculosis of the lungs occurred rarely.

Almost all of these hearts were large; they were often of enormous size, even in the absence of a valvular lesion. This was entirely, or almost entirely, due to a right-sided enlargement, dilatation exceeding hypertrophy in a disproportionate degree. The left side underwent relatively little change from narrowness to a moderate increase in size. The average heart weight for nineteen patients above the age of fourteen years was 574 gm., and in nine cases of complete or almost complete absence of valvular lesions it was 469 gm. There was some evidence that the size of the heart was influenced by the size of the interatrial defect. The pulmonary artery was always larger than the aorta, the average ratio being 3:2. Expressed in absolute figures, the pulmonary artery was large or very large, but rarely normal in size. The aorta was usually below the normal figures, often being very small and thin walled. The branches of the pulmonary artery were often dilated, the artery as well as its branches being the seat of atherosclerotic processes. As seen in situ, the right side of the heart formed the entire front wall; the pulmonary conus extended far to the left and upward, and the aorta was placed between the pulmonary artery and the superior vena cava.

This cardiovascular malformation can be best conceived in its entity by assuming that there was added to the congenital arrest of development an acquired

hydraulic disturbance, a shunt from left to right, as a result of which the right side of the heart and the lesser circulation handled an increased amount of blood and the left side of the heart and the greater circulation a decreased amount of blood. The indirect evidences for this theory were given.

The average age was thirty-six years; the prognosis as to duration of life was about equal with that in coarctation of the aorta, less than that in the interventricular septal defect and better than that in patency of the ductus arteriosus and pulmonary stenosis. Repeated pregnancies, anesthesia, and capacity for physical work were well supported in a number of cases; in others, however, chronic invalidism was present. The common combination with chronic valvular lesions did not aggravate the prognosis. There was prevalence of the female over the male sex in the proportion of 3:2, similar to the ratio in patency of the ductus arteriosus.

The clinical course was that of ordinary cardiac failure, lasting for shorter or longer, periods, even when all the cases with valvular complications were omitted. Clubbing was sometimes present. Cyanosis was more often present than not, but the combination with lesions of the mitral and tricuspid valves is to be remembered. Pallor, a small radial pulse, and a tendency to a lower blood pressure were rather common. These findings may be understood as an expression of actual arterial underdevelopment and/or a decreased output of blood into the greater circulation. Other clinical findings were an expression of the enormous right-sided enlargement of the heart. These were: the precordial bulge; certain features of the apical thrust (circumscribed and resistant, indefinite and systolic retraction); systolic propulsions and depressions of smaller or larger parts of the thoracic wall (important for differential diagnosis from chronic pericardial disease); the occurrence of a systolic or presystolic pulse in the veins and liver, which was influenced by venous fullness, the presence of sinus rhythm or auricular fibrillation; and the occurrence of regurgitation of the tricuspid and mitral valves. Auricular fibrillation was common; in this the interatrial septal defect distinguished itself entirely from all other congenital cardiovascular malformations in which auricular fibrillation was of the greatest rarity. The same cause obviously was responsible for auricular fibrillation and chronic valvular deformity, especially of the mitral orifice. The common occurrence of an accentuation of the pulmonary second sound was mainly an expression of a concomitant lesion of the mitral valve. In the absence of this lesion accentuation was sometimes present. Murmurs were at times absent. When present, however, they were more commonly due to the combination of valvular lesions. In the absence of lesions, there was still dilatation of the pulmonary artery to be considered with or without changes in the wall and relative insufficiency of the orifice as the cause of murmurs which were probably thought to be characteristic of the defect. If a characteristic murmur of this sort existed, it was midsternal systolic, probably partly diastolic and not accompanied by a thrill.

The roentgenologic findings were those of a large heart varying in shape from oval to globular and extending, as a rule, toward the left. The pulmonary conus and artery projected far to the left and upward and forward. The branches of the pulmonary artery (the "hili") at times showed increased pulsations and were sharply defined and enlarged. Lack of knowledge of the roentgenologic picture led to the erroneous diagnosis of mediastinal tumor or tuberculosis. The aortic knob was small—at times invisible. Other conditions which caused pulmonary dilatation and narrowness or absence of the aortic knob were given.

The interesting finding from the electrocardiographic study was the presence, as a rule, of only a moderate degree of axis deviation to the right. Enormous dilatation of the right side of the heart with comparatively moderate hypertrophy did not cause a high degree of right axis deviation in the electrocardiogram.

Weiss, Soma, and Ferris, Eugene B., Jr.: Adams-Stokes Syndrome With Transient Complete Heart-Block of Vagovagal Reflex Origin. *Arch. Int. Med.* 54: 931, 1934.

This study centers around observations on a patient who for ten years suffered from attacks of fainting precipitated usually by the swallowing of food. The patient had a traction diverticulum of the esophagus, distention of which with the aid of a rubber balloon promptly induced auriculoventricular dissociation of the heart and syncope. The release of pressure in the balloon was associated with a prompt return of normal sinus rhythm and the disappearance of symptoms. The Adams-Stokes attack in this case was induced by heart-block precipitated by a vagovagal reflex. The source of the reflex was irritation of the sensory endings of the vagi by the diverticulum.

Various studies on blood flow and the effects of drugs on the attacks of heart-block are reported. The relative rôle of organic cardiac lesions and of neurogenic factors in the precipitation of Adams-Stokes attacks with heart-block is discussed and the simultaneous presence of multiple etiologic factors is stressed.

Weiss, Harry: Relation of Portals of Entry to Subacute Bacterial Endocarditis. *Arch. Int. Med.* 54: 710, 1934.

Results of a study of 364 cases of subacute bacterial endocarditis suggest that the common portal of entry of the streptococcus is from foci of infection in the passages of the upper respiratory tract and the mouth. Other portals of entry are the genitourinary tract, otitic infections, and wound infections. There is no evidence of the gastrointestinal tract as the portal of entry in any of the cases. The onset with an acute infection of the upper respiratory tract or tonsillitis in many cases led to the conclusion that in these apparently benign infections a transient bacteremia may occur. The frequency of antecedent cardiac disease, usually rheumatic but sometimes atherosclerotic or syphilitic, or some congenital lesion, indicated that the streptococcus probably requires a previously diseased or abnormal endocardium on which to implant itself.

Ten cases of subacute bacterial endocarditis are reported in which a history of tonsillectomy or extraction of a tooth closely antedated the onset of symptoms, indicating that trauma of an infective focus about the teeth and pharynx may produce transient bacteremia and thus play a part in promoting implantation on the endocardium.

Hamman, Louis: Sudden Death. *Bull. Johns Hopkins Hosp.* 55: 387, 1934.

Among the many causes of this phenomenon the author believes three are the most important. These are: sudden stopping of the heart, hemorrhage, and arterial embolism and thrombosis. Death due primarily to cardiac standstill occurs under two different circumstances: first, when the heart after a prolonged struggle against overwhelming difficulties finally plays out; second, when the heart while satisfactorily performing its work suddenly stops. Death due to the first cause can hardly be called sudden, since the overwhelming difficulties usually have been present sufficiently long to give warning of the impending end.

The author describes the second cause of sudden stopping of the heart as being due probably to ventricular fibrillation. He believes this condition occurs more frequently than is generally recognized and that many unexplained sudden deaths are due to this disturbance of mechanism. This probably is particularly true in those cases in which very little anatomical change can be found in the heart muscle at autopsy. Often only slight changes are found in the myocardium, small areas or scarring of a small infarct, and yet, these apparently trivial lesions may perhaps be enough to inaugurate the fatal rhythm.

Considerable space is given to the diagnosis of the causes of sudden death.

ABSTRACTS

Fishberg, Arthur M., Hitzig, William M., and King, Frederick H.: *Circulatory Dynamics in Myocardial Infarction*. Arch. Int. Med. 54: 997, 1934.

Fifty-nine patients with recent myocardial infarction were studied from the point of view of circulatory dynamics. The venous pressure was measured in all, the circulation time in thirty-eight and the volume of circulating blood in twenty-nine of the subjects.

Two distinct mechanisms participate in the derangement of the circulation in myocardial infarction: (a) shock, or peripheral circulatory failure, which diminishes the venous return to the heart and tends to lower the pressure in the large systemic veins; and (b) heart failure, which tends to engorge the pulmonary circuit in consequence of insufficiency of the left side of the heart and to raise the systemic venous pressure in proportion to the insufficiency of the right side of the heart.

In initial myocardial infarction in persons without previous severe heart failure, the clinical picture is most often predominantly that of shock. The venous pressure is then subnormal. The blood flow through the lungs is slowed but little, if at all. The volume of circulating blood tends to be diminished.

When infarction affects patients with previous heart failure, the manifestations of either shock or cardiac insufficiency may be predominant. When heart failure dominates, the venous pressure is elevated or normal, the flow of blood through the lungs is retarded, and the volume of circulating blood is increased.

The diminished venous return due to shock lessens the work of the heart and thus militates against the development of cardiac insufficiency. It is because of this diminution in the venous return to the heart that engorgement of the lungs and systemic veins may be absent despite extensive myocardial infarction.

The fall in arterial pressure is due not only to the weakness of the left ventricle but also to the peripheral circulatory failure of shock. Apparently the latter is usually the more important of the two factors. It is because of concomitant presence of shock that a fall in the arterial pressure is so much more prominent in myocardial infarction than in other lesions of the heart.

Statistically, the immediate prognosis of myocardial infarction is better with low than with high venous pressure.

The type of circulatory failure present is of significance for the rational treatment of patients with myocardial infarction.

Wayne, E. J., and Graybiel, Ashton: *Observations on the Effect of Food, Gastric Distention, External Temperature, and Repeated Exercise on Angina of Effort, With a Note on Angina Sine Dolore*. Clin. Sc. 1: 287, 1934.

An average reduction of 25 per cent in exercise tolerance occurred after a heavy meal in six patients with pure angina of effort. In the same six patients, exercise tolerance was unaffected by inflation of the stomach with air, even when sufficient was introduced to give epigastric discomfort and to displace the heart. It is concluded that in angina of effort the reduction of exercise tolerance after food is due to the increased energy expenditure of the heart and not to gastric distention. In normal individuals large amounts of air were introduced into and retained by the stomach. While the stomach was distending, slight changes in pulse and blood pressures occurred, but, when the stomach had adapted itself, no changes in the cardiovascular system could be detected even though the heart was mechanically displaced.

A case of spontaneous angina is described in which both food and gastric inflation gave rise to attacks; it is considered likely that distention of the stomach can reflexly initiate an attack of this type of case.

Variations in the external temperature did not affect exercise tolerance in six patients with angina of effort. Two types of angina of effort exist; in both, exercise tolerance is constant if sufficient rest is allowed between the end of one attack and the start of the next test. In one type, as this period of rest is reduced, exercise tolerance gradually diminishes; in the other, there is a phase which may be as long as an hour, during which exercise tolerance is increased. Diminishing the rate of exercise had no effect in two patients, and in four gave a moderate increase in the total amount of exercise performed.

A case is described in which the symptoms resembled those previously described under the term "angina sine dolore." Investigation showed that the attacks were due to paroxysmal ventricular action brought on only by exercise. The conception of "angina sine dolore" is briefly discussed.

Poynton, F. J.: *Some Aspects of Heart Disease in Childhood*. Bristol Med.-Chir. J. 51: 205, 1934.

In this Long Fox Memorial Lecture, the author describes the various forms of heart disease occurring in children, including tuberculous and meningococcal heart disease. He reviews his own previous work and ideas developed a good many years ago and correlates them with the findings of heart disease at the present time. He particularly emphasizes the importance of apyrexial carditis and states that this form is repeatedly seen in children under the age of five years. In his own study he has found the incidence to be about 10 per cent. He also states that the mortality at this age is proportionately greater than at any period.

He discusses particularly the etiology of heart disease at this time of life and points out the difficulty in correlating the finding of rheumatic carditis with malignant endocarditis.

Pickering, G. W., and Wayne, E. J.: *Observations on Angina Pectoris and Intermittent Claudication in Anemia*. Clin. Sc. 1: 305, 1934.

Pains clinically indistinguishable from those of intermittent claudication and angina pectoris may occur in any type of severe anemia. Of twenty-five consecutive ambulatory cases of severe anemia, seven complained of pain in the legs and eight of pain in the chest induced only by exercise and relieved by rest. After cure of the anemia only one patient experienced pain in the legs and two pain in the chest. In nine patients grossly anemic, exercise of the limbs without circulatory arrest produced severe pain having the characteristics of intermittent claudication. After cure of the anemia similar exercise produced no or only slight pain. After a given amount of exercise, blood flow through the active muscles is at least as great in the anemic as in the nonanemic state. It is suggested that the stimulus which produces the pain of intermittent claudication is an accumulation in the tissue spaces of metabolites normally removed by oxidation.

In six severely anemic patients, complaining of sternal pain or tightness on walking, the sensation was reproduced by exercise tests. In four patients, the same exercises no longer produced pain or tightness when the blood contained more than 50 per cent of hemoglobin. In two patients, the exercise tolerance increased with rising hemoglobin content of the blood, but pain could still be induced when the blood was normal. The reaction of heart rate and blood pressure to exercise is usually altered in anemia, and such alterations may contribute to the development of anginal pain. It is concluded, however, that the essential factor in the production of anginal pain is a diminished oxygen supply to the working heart muscle.

ABSTRACTS

These observations support the view that angina pectoris and intermittent claudication are due to similar mechanisms operating in the heart and skeletal muscles. Reasons are given why some, but not all, anemic patients complain of angina or of intermittent claudication.

No electrocardiographic changes characteristic of myocardial anoxemia were detected in anemic patients after exercise. In two patients the P-R interval was abnormally long in the anemic state and was within normal limits after cure of the anemia.

Berlin, David D., Blumgart, H. L., Weinstein, A. A., Riseman, J. E. F., and Davis, David: Treatment of Angina Pectoris and Congestive Failure by Total Ablation of the Normal Thyroid Gland. *New England J. Med.* 211: 863, 1934.

The present report deals with three surgical problems in the technic of the operation for total ablation of the thyroid gland. The value of the various anesthetics is also discussed. In seventy-five operations, there have been three permanent unilateral nerve injuries. No severe manifestations of parathyroid insufficiency have occurred in this group. Two patients still require calcium therapy, but their symptoms are completely controlled. By modification in pre- and postoperative treatment, improvement in surgical technic and by the use of local anesthesia, the last thirty-six consecutive patients with chronic heart disease have been operated on without mortality.

The results of total thyroidectomy for the treatment of chronic rheumatic heart disease are reported and compared with those obtained in the treatment of arteriosclerotic heart disease. Twenty-nine patients have been treated by total thyroidectomy. Of these, twenty-five had congestive failure, three had congestive failure and angina pectoris, one had angina induced by paroxysmal auricular fibrillation, and one had congestive failure and rapid heart action.

The incidence of good results was somewhat greater in these patients with rheumatic heart disease than in those with arteriosclerotic heart disease. Although it is difficult to be certain of all the factors which account for the differences of two such dissimilar groups of patients, certain considerations are worthy of mention. The preoperative basal metabolic rate is more likely to be normal or higher in the rheumatic group than in the arteriosclerotic group, and it has been shown that the higher the metabolic rate, the greater will be the relief following total thyroidectomy. Also a history of previous coronary thrombosis will limit the satisfactory results following thyroidectomy. Since coronary thrombosis is rare in rheumatic heart disease, this factor will seldom require consideration in such patients. The patients with arteriosclerotic heart disease were definitely older, and these patients are more subject to cerebral hemorrhage or thrombosis as well as coronary thrombosis, and for this reason the ultimate results are not so satisfactory as the results in the group of rheumatic heart disease which was definitely younger.

Cassio, P., and Berconsky, I.: Non-apparent Cardiac Insufficiency. *Rev. Argentina de Cardiologia* 1: 11, 1934.

An analysis of the blood, respiratory and circulatory functions in twenty-seven patients with diverse cardiovascular disturbances but showing none of the symptoms of cardiac insufficiency (dyspnea, visceral congestion, etc.) showed that about 80 per cent of these patients had a decreased efficiency of the heart as a pump. The authors suggest the name of nonapparent (inapparent) cardiac insufficiency to designate this condition, to indicate that the cardiac insufficiency is not easily recognized by the ordinary methods of examination.

The authors believe that these patients may have a diminished efficiency of the heart in spite of the absence of either respiratory or visceral congestion.

and show this by an increased heart rate, a lowered pulse pressure, and especially definite enlargement of the heart. These findings should indicate a structural alteration of the cardiovascular system. If a lowered velocity of blood flow, an increased difference in the venous and arterial oxygen content, and decreased vital capacity, etc., are found, this diagnosis will be confirmed.

The authors conclude from their study that digitalis should be prescribed for these patients suffering from nonapparent cardiac insufficiency in order to delay the possibility of its becoming an apparent one.

Page, Irvine H., and Heuer, George J.: A Surgical Treatment of Essential Hypertension. *J. Clin. Investigation* 14: 22, 1935.

Section of the anterior nerve roots from the sixth thoracic to the second lumbar segment has been performed in a young girl suffering from persistently elevated arterial blood pressure. Anatomical and physiological evidence indicated that her vascular system was yet flexible.

The blood pressure level quickly fell to normal and has remained normal for seven months.

Denervation of the kidneys resulting from the operation did not alter their power to excrete urea, but there was slight loss in ability to concentrate urine. The kidneys were as efficient when the blood pressure was reduced to normal as when it had been elevated. No increase occurred in the number of red blood cells excreted in the urine.

In spite of the fact that the blood pressure fell to normal, there was no change in the subjective feeling of the patient except that headaches, palpitation, and the precordial pain disappeared.

No significant alterations occurred in the hemoglobin and plasma proteins. The basal metabolism and cardiac output also were normal. Electrocardiographic records taken before and after operation showed no change from normal.

Determinations were made of total lipid, total and free cholesterol, lipid amino nitrogen, total lipid nitrogen, and lipid phosphorus in the blood plasma both before operation, when the blood pressure was elevated, and after, when it was normal. Except for slight rise in lipid amino nitrogen and total lipid nitrogen following operation, the changes were insignificant.

Page, Irvine H., and Heuer, George J.: The Effect of Renal Denervation on the Level of Arterial Blood Pressure and Renal Function in Essential Hypertension. *J. Clin. Investigation* 14: 27, 1935.

Bilateral renal denervation in a patient suffering from severe essential hypertension did not change the level of arterial blood pressure; hence the results give no ground for expecting that denervation in cases of essential hypertension is of therapeutic value. No ill effects either renal or extrarenal were observed after denervation. Renal efficiency as measured by the urea clearance test and the ability of the kidneys to concentrate was normal before operation and remained unchanged after denervation. The results do not support the hypothesis that essential hypertension originates in whole or in part in the nervous mechanism of the kidneys.

Friedlander, Richard D., and Levine, Samuel A.: Auricular Fibrillation and Flutter Without Evidence of Organic Heart Disease. *New England J. Med.* 211: 624, 1934.

An analysis has been made of thirty-five cases of auricular fibrillation and four cases of auricular flutter in which no other signs of cardiac disease were demonstrable and in which rheumatic heart disease, coronary artery disease, hy-

pertension, hyperthyroidism and syphilis could not be considered contributory. These cases composed approximately 6 per cent of all patients with auricular fibrillation and 20 per cent of all those seen with auricular flutter during the same number of years in private practice.

Of the thirty-five cases of auricular fibrillation, thirteen were classified as transient and twenty-two as permanent. Less than half of the patients in the entire group were over fifty years of age, and there were only three females in all.

In those cases with transient auricular fibrillation, the average at the onset was thirty-two years for those under fifty years of age and fifty-two years for those over fifty years of age. In the patients with permanent auricular fibrillation, the averages were forty-seven years and fifty years for the two age groups.

The blood pressure, basal metabolism, vital capacity, and laboratory findings were considered to be within normal range for the entire series. Cardiac examinations were entirely negative in all. Roentgenograms were obtained in one of the transient cases and in nine of the permanent group and, except for very slight cardiac enlargement in one case in each group, were considered negative.

The inciting factor was elicited in nine of the patients with transient fibrillation and somewhat less definitely in six of those in the permanent group. Included in these incitants in the order of frequency were exertion, gastrointestinal disturbances, alcohol, and upper respiratory infections.

Experiences with treatment in this small group of cases would seem to indicate that digitalis may diminish the frequency of transient attacks of fibrillation, but is practically ineffective in restoring normal rhythm in the permanent group. Quinidine is generally effective in establishing a normal rhythm in this latter group.

All the patients with auricular flutter were males, three of whom were over sixty years of age, the other was thirty-eight years old. Cardiac examinations were negative in all. Pneumonia in one patient and exertion in two of the others were the only possible inciting factors. No conclusions can be drawn regarding the effect of medication in this small group of cases, except that digitalis restored the rhythm to normal in two of the patients and quinidine in another.

The assumption has been made that in such cases as these under discussion, the mode of onset of the irregularity may be the result of a "trigger" mechanism of neurogenic origin in certain otherwise normal individuals with hyperreactive or unstable nervous systems. This mechanism may be related to that associated with the onset of similar arrhythmias in hyperthyroidism.

This study emphasizes the fact that auricular fibrillation and flutter must be regarded in some cases as benign or functional arrhythmias.

Thomson, William A. R.: *The Plasma Proteins and Cardiac Edema*. Quart. J. Med. 3: 587, 1934.

The results are recorded of an investigation of the plasma proteins in fifty-four patients, consisting of eighteen cases of heart failure with edema, sixteen cases of heart disease accompanied by edema, six cases of Bright's disease, four cases of tuberculosis, a miscellaneous group of seven cases and three junior members of the hospital staff who were used as normals. In all, eighty-seven estimations were made.

There is a distinct diminution in the plasma proteins in cardiac edema, 87.5 per cent of the cases having a plasma albumin content of less than 3.2 gm. per cent. In heart disease without edema, there is only a slight diminution in the plasma proteins as compared with the normal, 87 per cent of the patients having a plasma albumin level greater than 3.2 gm. per cent.

In view of these findings it is suggested that plasma protein deficiency plays an important rôle in the etiology of cardiac edema. The main cause for the plasma protein depletion in cardiac edema is considered to be malnutrition. It is suggested that the dietary of patients with cardiac edema should contain the maximum amount of protein compatible with their digestive powers.

Lewis, Thomas, and Pickering, G. W.: Observations Upon Maladies in Which the Blood Supply to Digits Ceases Intermittently or Permanently and Upon Bilateral Gangrene of Digits; Observations Relevant to So-Called "Raynaud's Disease." Clin. Sc. 1: 327, 1934.

The purpose of the paper is to show that a number of distinct conditions have been described under the term "Raynaud's disease," separately to explore these, and to indicate directions in which new inquiries may be conducted. It is considered that the term "Raynaud's disease" should be abandoned.

The present inquiries again point to the existence of a local fault as a cause of both Raynaud's disease and of bilateral gangrene. The several causes of local faults of the vessels are enumerated:

Intermittent spasm of digital arteries with generalized scleroderma.

Raynaud's phenomenon arising out of local injury, including the use of vibrating tools.

Bilateral gangrene of digits in the young, and with infection; this condition is regarded as probably the result of thrombotic closure of vessels.

Bilateral gangrene with hemoglobinuria from cold, a condition having probably a unique pathogeny.

Bilateral gangrene of digits in the elderly, in which closure is shown to be thrombotic but preceded by disease of the small arteries.

Thromboangitis obliterans associated with Raynaud's phenomenon.

Cervical rib or crutch pressure causing Raynaud's phenomenon or gangrene, so it is thought, by thrombotic and embolic processes.

It is suggested that gangrene is never the result of uncomplicated spasm of arteries. Evidence tends increasingly to show that gangrene depends upon structural occlusion of the vessels.

Pickering, G. W.: The Cerebrospinal Fluid Pressure in Arterial Hypertension. Clin. Sc. 1: 397, 1934.

The general clinical features presented by hypertensive patients with cerebrospinal fluid pressures of 250 mm. water and over contrast strongly with those presented by patients having lower pressures. The former are younger, the kidneys are usually severely damaged, and the disease progresses rapidly to a fatal termination. The latter are older, the kidneys usually escape severe damage, and the disease progresses less rapidly.

Every patient with a cerebrospinal fluid pressure over 250 mm. water developed albuminuric retinitis. With one exception, every patient with a lower cerebrospinal fluid pressure had either no retinal lesion or the lesions characterizing arteriosclerotic retinitis. It is suggested that the essential difference between these two forms of retinitis is the addition in the albuminuric type of neuroretinal edema resulting from increased intracranial pressure.

In individual patients with high blood pressure, the cerebrospinal fluid pressure has been found unaltered during headache and during acute attacks of coma and convulsions unassociated with uremia.

There is a relation between high diastolic blood pressure and high cerebrospinal fluid pressure, and it is suggested that the former is one of the factors determining the latter.

Book Reviews

DAS BERIBERI-HERZ: MORPHOLOGIE, KLINIK, PATHOGENESE. By Professor K. F. Wenkebach, in charge of the First Medical University Clinic in Vienna. Julius Springer, Berlin and Vienna, 1934, 106 pages, with 38 illustrations.

Professor Wenkebach's monograph on the beriberi heart is the outcome of an invitation visit to Java; and the book reflects his great interest in this problem, as well as in other types of heart disease, and the friendly cooperation of the men with whom he worked. Even in our own part of the world where beriberi, far from being an important public health problem, is a rarity, the study should be read with great interest. "Shôshin," the rapidly fatal affection of the heart which appears in some cases of beriberi, presents a striking clinical picture—the picture of a rapidly developing and extreme degree of pure right-sided failure unassociated with valvular damage or with evidences of failure of the left ventricle. The patient is seen complaining of severe epigastric and retrosternal pain, writhing and tossing in bed, equally distressed whether erect or reclining, breathing rapidly and superficially; the veins and liver are tremendously enlarged and pulsating, and the lungs are free from any sign of congestion. After focussing the reader's attention on the clinical picture of shôshin Professor Wenkebach presents the gross and microscopic anatomy, the characteristic x-ray picture, and the heart of infants affected with beriberi. He then describes some of the physical signs in greater detail, stressing particularly the enormous enlargement of the heart, the peripheral vascular signs, and the remarkable response to certain hormones. There is a prompt exacerbation of all symptoms upon the injection of adrenalin and an equally prompt improvement following the injection of pitressin; the results of which are so dramatic that the former drug is used as a diagnostic aid to measure improvement during convalescence, and the latter is considered as of possible therapeutic value. In the final section of the study the author takes up certain theoretical considerations—the nature of the water retention, which differs from edema, the relation between muscle tonicity and contractility, the disproportion between the involvement of the right and left sides of the heart, the basis underlying the vascular signs, the part played by the glands of internal secretion, the relation between the nervous manifestations and the disturbance of the skeletal and cardiac muscles. These are fundamental problems, of great interest and importance whether or not we ever see a case of beriberi heart.

E. H.

ENFERMEDADES DEL PERICARDIO. By Dr. Carlos P. Waldorp and Dr. Samuel Genioviehi. Anieto Lopez, Buenos Aires, 1934.

This volume of more than four hundred pages represents a praiseworthy attempt to cover the entire field of diseases of the pericardium. The book is systematically arranged and freely illustrated. Most of the subjects are covered adequately.

The extensive bibliography loses some of its value because neither the volume nor the page is given in the references.

The book should find a distinct field of usefulness in Spanish-speaking countries.

L. A. C.

PHYSIOLOGY IN HEALTH AND DISEASE. By Carl J. Wiggers, M.D., Professor of Physiology in the School of Medicine of Western Reserve University, Cleveland, Ohio. Lea & Febiger, Philadelphia, 1,184 pages, with 182 illustrations.

To all those familiar with Dr. Wiggers' classic monograph, *The Circulation in Health and Disease*, the plan and character of the new volume will at once be apparent. He has extended to the whole field of human physiology the method employed in his earlier book on the circulation.

It is obvious that the plan of presenting side by side the normal and the pathological aspects of physiology has many and great advantages to every one—student, general practitioner, and clinician—whose interest in physiology lies primarily in its application to the problems of clinical medicine.

In this treatise of some 1,200 pages, almost 300 pages are devoted to the section on "Heart and Circulation." This portion of the new book follows the general lines of the author's earlier one, although the section has been entirely rewritten and extensively revised. The text of this section has been condensed to about one-half that of the earlier book; but in spite of this, much important new material has been added. The recent advances concerning the peripheral blood vessels are fully recorded, and there is a new and admirable chapter on the coronary circulation and its disturbances. Indeed, throughout the entire volume there is constant evidence of the effort to bring the whole field of physiological knowledge into relationship with the everyday problems of clinical medicine.

The appearance of Dr. Wiggers' book is an event of the first importance to every one interested in tightening the bonds between physiology and the clinical sciences.

L. A. C.

THE HEART VISIBLE. A CLINICAL STUDY IN CARDIOVASCULAR ROENTGENOLOGY IN HEALTH AND DISEASE. By Dr. J. Polevski, Attending Physician and Cardiologist, Newark Beth Israel Hospital. F. A. Davis Company, Philadelphia, 1934, 207 pages, with 122 illustrations.

In the preface Dr. Polevski states that this book is intended for the radiologist who has the scientific curiosity of a clinician and also for the cardiologist and for every clinician eager for any and every possible means that will enable him to establish a diagnosis that will be in keeping with the facts. He might also add that the book would be suitable for the medical student who is interested in learning the first principles of the fluoroscopic examination of the heart and great vessels. The text is simply written and generously illustrated, and the illustrations have been carefully selected and well printed so that they really illustrate. The author stresses the value of careful observation, not only in the anteroposterior position, but also in the oblique and lateral positions, and one might wish that he had chosen to show more of the oblique views of the chest, particularly in relation to the study of the aorta and the distinction between dilatation and tortuosity. The work is useful in calling attention to a method of investigation which has not been sufficiently utilized, in illustrating the appearance of the cardiac silhouette under normal and abnormal conditions, and in discussing various extrinsic factors which if not properly interpreted may lead to mistakes in diagnosis. It probably contains little that is not familiar to the radiologist and the cardiologist for whom it was intended.

E. H.

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Original Communications

ASYNCHRONISM IN CONTRACTION OF THE VENTRICLES IN THE SO-CALLED COMMON TYPE OF BUNDLE-BRANCH BLOCK: ITS BEARING ON THE DETERMINATION OF THE SIDE OF THE SIGNIFICANT LESION AND ON THE MECHANISM OF SPLIT FIRST AND SECOND HEART SOUNDS*†

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THE views of Eppinger and Rothberger² and Lewis³ regarding the electrocardiographic localization of the side of the significant lesion in bundle-branch block, which were based on animal experimentation, have not been universally accepted as applicable to man.^{4, 5, 6} The opponents of these views have pointed out that the different anatomical relations in man as compared with dogs render unsafe generalizations regarding the conducting apparatus in man from data obtained in dogs. The evidence resulting from serial sections of the A-V conduction system in cases which had exhibited bundle-branch defects is apparently conflicting.⁷⁻¹¹ There are, however, very few cases reported in which (1) the electrocardiograms conform strictly to the criteria of bundle-branch block, and (2) histological studies are adequate. The data obtained by (a) experimental production of extrasystoles in man,¹² and (b) studies on the order of ventricular excitation in bundle-branch block by the use of semidirect leads⁶ have led Wilson and his coworkers to conclusions directly opposite to those of Eppinger, Rothberger and Lewis. Recently, doubt has been cast on the validity of the conclusions of Wilson and his group by Katz and Ackerman,¹³ who have demonstrated in dogs the importance of comparatively slight changes of position of the heart on the direction of

*Presented in part before the Association of American Physicians, May 9, 1933.¹

†From the Robinette Foundation, Medical Division, Hospital of the University of Pennsylvania.

the QRS complex. These observers believe that it is unjustifiable to attempt to localize the site of the bundle-branch block from the direction of the major initial complex of the three leads of the electrocardiogram.

It is desirable for the development of our knowledge of electrocardiographic localization of myocardial damage, that the side of the lesion in the common type of bundle-branch block be determined beyond doubt. It occurred to us that new evidence bearing on the problem might be obtained by studying the time relations of various phenomena related to ventricular contraction on the two sides of the heart. The hypothesis that asynchronism in contraction of the two ventricles may occur is not new.* Before the advent of electrocardiography, some writers maintained that reduplication of the first sound is due to asynchronism in the beginning of contraction of the two ventricles. This idea has received little, if any, support in recent years,

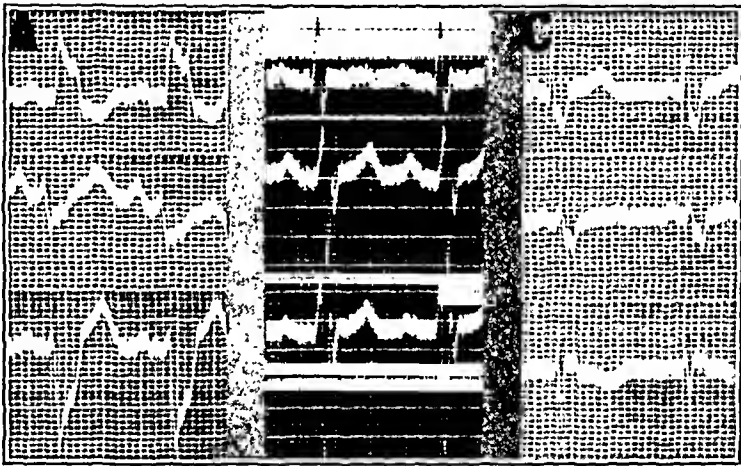


Fig. 1.—A, The common type of bundle-branch block.

B, Case J. O.C. (Table IV). A relatively uncommon type of intraventricular conduction defect.

C, Case A. O. (Table IV). This type of intraventricular conduction defect ranks second in frequency to the common type. The significant lesion probably involves the conduction system on the right side.

although no actual evidence opposed to it has been presented. As far as we know, it has never been tested in man. Most clinicians probably believe that reduplication of the second heart sound is due to asynchronous closure of the aortic and pulmonic valves, but no adequate proof has been available.

Katz¹⁵ has shown in experimental animals that there is often slight asynchronism in the beginning and ending of the ejection periods from the two ventricles. The frequency with which splitting of both first and second heart sounds is noted in bundle-branch block and the reported finding of a bifid systolic apex impulse¹⁶ suggest that these phenomena might be due to asynchronous contraction of the

*This subject has been reviewed by Holt.¹⁴

two ventricles. Moreover, such a hypothesis seems reasonable, because, according to the generally accepted explanation for the mechanism of bundle-branch block, the excitatory process is delayed in reaching the ventricle on the side of the block. The response might therefore also be delayed.

In the present study, the time relations of various events associated with right and left ventricular contraction were studied in a series of patients, whose electrocardiograms conformed rigidly to accepted criteria for the so-called common type of bundle-branch block (Fig. 1A).

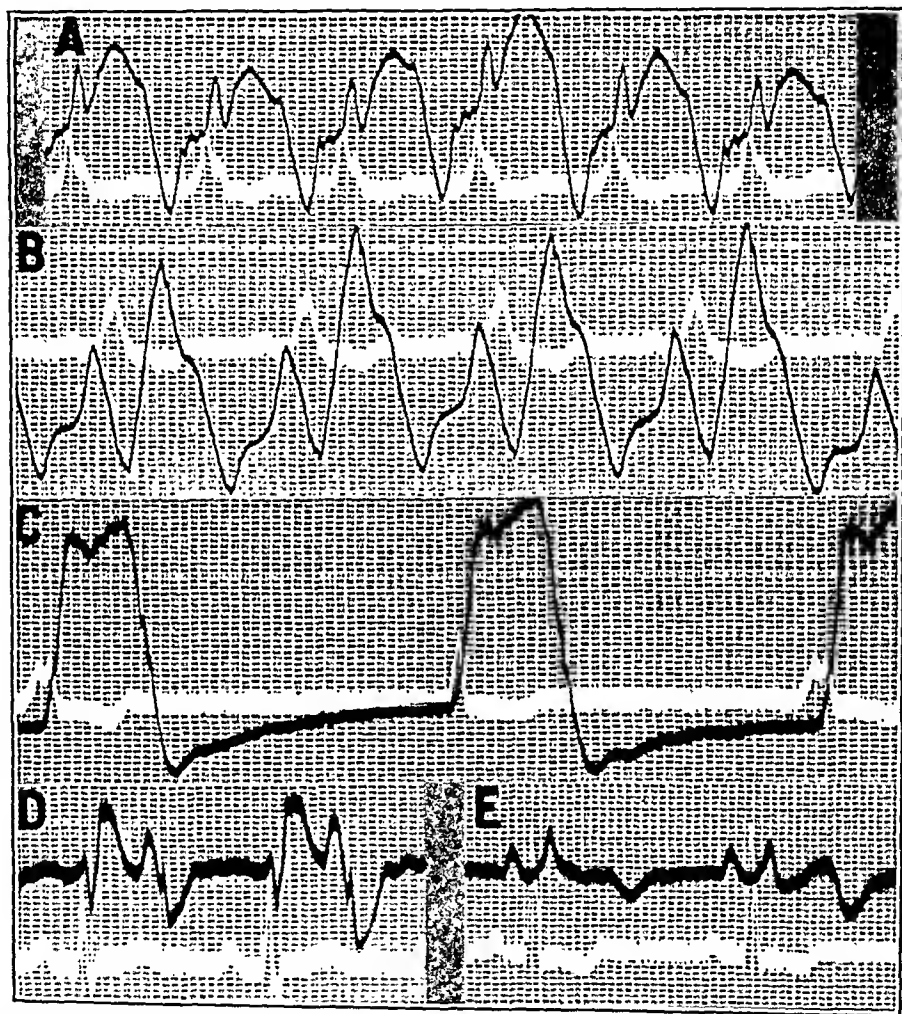


Fig. 2.—Various types of apex impulse in cases with bundle-branch block and cases without bundle-branch block.

A, Case R. B. (Table 1). Bifid apex impulse in the common type of bundle-branch block, both components beginning during the period of ventricular systole.

B, Case R. J. Bifid apex impulse in the common type of bundle-branch block, one component beginning before and one during ventricular systole.

C, Case H.H. (Table 1). Single apex impulse in the common type of bundle-branch block (first and third beats). The second beat illustrates the occasional recovery from bundle-branch block which occurred in this patient. While the contour of the apex impulse is similar in both types of beats, its onset is considerably retarded in the beats showing bundle-branch block.

D, Bifid apex impulse in a patient with normal intraventricular conduction time. Both components occur during ventricular systole.

E, Bifid apex impulse in a patient with normal intraventricular conduction time. The first component of the bifid impulse precedes ventricular systole.

All the cases in this series, so classified, had the following electrocardiographic characteristics: (1) the QRS complexes had a duration of not less than 0.14 of a second in at least one lead; the amplitude of the QRS complex in Lead I was at least 6 mm. and in Lead III was always greater; (2) the main QRS complex was upward in Lead I and downward in Lead III; (3) the terminal or T-deflection was downward in Lead I and upward in Lead III.

The methods used for determining the various time relations under consideration included (1) various combinations of electrocardiograms, sound tracings,* optically recorded apex cardiograms, carotid artery and venous pulse tracings with the recording devices arranged to avoid parallax and (2) roentgenkymographic tracings of the aortic and pulmonary artery pulsations, timed by superimposition of the 60 cycle x-ray current disturbance on an electrocardiogram.

APEX CARDIOGRAMS

Optically recorded apex cardiograms timed by electrocardiograms (care being taken to exclude parallax) were obtained in 5 cases with the common type of bundle-branch block. Three of these cases exhibited a bifid outward thrust in early systole (Fig. 2A), one a bifid

TABLE I

TIME INTERVALS BETWEEN THE BEGINNING OF THE QRS COMPLEX OF THE ELECTROCARDIOGRAM AND THE OUTWARD THRUST OF THE OPTICALLY RECORDED APEX IMPULSE

THE COMMON TYPE OF BUNDLE-BRANCH BLOCK		NORMAL INTRAVENTRICULAR CONDUCTION AND GOOD CARDIAC FUNCTION		NORMAL INTRAVENTRICULAR CONDUCTION AND DECOMPENSATION	
CASE	TIME INTERVAL (SECOND)	CASE	TIME INTERVAL (SECOND)	CASE	TIME INTERVAL (SECOND)
W. B.	0.05	E. C.	0.05	K. M.	0.06
H. P.	0.04	F. R.	0.03	H. G.	0.06
R. B.	0.05	P. G.	0.04	L. B.	0.03
L. H.	0.05	S. W.	0.02	W. H.	0.04
H. H.*	0.05 to 0.08	K. H.	0.04	A. R.	0.05
(auricular fibrillation)	(During bundle-branch block and 0.02 (in beats with normal QRS complexes)	O. G.	0.02	L. Y.	0.04
		A. E.	0.04	W. W.	0.03
		E. M.	0.04	J. G.	0.04
		C. P.	0.03	G. M.	0.06
		J. G.	0.04	A. D.	0.06
Average	0.048		0.035		0.047

*The systolic thrust was single in both types of beats (see Fig. 2 C). This case is excluded from the averages because of the presence of auricular fibrillation and consequent variability in duration of intervals between the QRS complex and the beginning of the apex thrust.

thrust the first component of which preceded ventricular systole (Fig. 2B), and one a single large apex thrust (Fig. 2C). The time interval between the beginning of the QRS complex and the beginning of the

*The method of sound recording has been previously described.²⁵

outward systolic thrust at the apex was essentially the same in cases of bundle-branch block as in a series of cases with cardiac decompensation. In normal controls the average duration of the interval was slightly less, although the differences could not be regarded as significant (Table I).

A study of the details of apex cardiograms obtained from controls without bundle-branch block, or even intraventricular conduction defect, reveals the fact that some of these cases also have a bifid outward thrust at the apex during systole (Fig. 2D). Whether this is a manifestation of asynchronism in some early phase of cardiac contraction cannot be stated at present. The data, although limited, appear to warrant the following statements: (1) A systolic bifid apex impulse is not always recorded in the common type of bundle-branch block; (2) a systolic bifid apex impulse is sometimes recorded in cases without intraventricular conduction defect; therefore (3) a systolic bifid apex impulse is not to be depended on as a sign of bundle-branch block.*

The outward thrust at the apex does not enable one to differentiate, with certainty, movement due to contraction of one or the other ventricle. Furthermore, because of variability in (1) rotation, (2) the relation of the heart to the chest wall, and (3) the duration of the isometric contraction phase, there is no certainty that the outward thrust of the heart has a fixed time relation to either the beginning of contraction or ejection from the ventricles. For these reasons the method was abandoned for the study of our present problem.

THE TIME OF APPEARANCE OF THE PULSE IN THE RIGHT CAROTID

The appearance time of the sharp primary oscillation in the right carotid artery pulse wave offers a fairly accurate criterion for determining the beginning of ejection from the left ventricle.¹⁷ According to reported studies of pulse wave velocity in large arteries, it may be calculated that this primary oscillation begins from 0.015 to 0.025 second after the beginning of ejection from the left ventricle. The measurements of the time intervals between the beginning of the QRS complex and the beginning of the right carotid artery pulse wave in Table II were obtained from tracings in which the electrocardiographic and optically recorded carotid pulse tracings were made simultaneously, care being taken to avoid parallax. The material comprised eleven cases of the common type of bundle-branch block, ten normal controls, and seven cases of cardiac decompensation. Care was taken to include among this group of controls only cases with a single first sound, because of the possibility that splitting of the first sound may be due to asynchronism in some phase of the early part of contraction. Reference to Table II reveals the fact that although

*J. K. Lewis²² in a study of apex cardiograms in 14 patients with bundle-branch block described them as "normal" in 9, as having a presystolic or protodiastolic impulse in 4, and a double systolic impulse in one.

there was a considerable range in the duration of the interval in control cases, it was significantly prolonged in all cases with the common type of bundle-branch block.* Comparison of the interval in the bundle-branch-block group with the interval in the cardiac decompensation controls, shows that the prolongation of the former cannot be accounted for by feebleness of the heart action. As a matter of fact, most of the patients with bundle-branch block had relatively good compensation and several of them were working.

TABLE II

TIME INTERVAL BETWEEN BEGINNING OF QRS COMPLEX AND BEGINNING OF RIGHT CAROTID ARTERY PULSE WAVE

THE COMMON TYPE OF BUNDLE-BRANCH BLOCK			NORMAL CASES WITH SINGLE FIRST SOUNDS		CASES WITH SINGLE FIRST SOUNDS AND CARDIAC DECOM- PENSATION	
CASE	RATE	INTERVAL (SECOND)	RATE	INTERVAL (SECOND)	RATE	INTERVAL (SECOND)
R. J.	75	0.16 (0.13)†	55	0.10	102	0.10
M. R.	80	0.16 (0.13)† (0.20)‡	74	0.10	108	0.13
R. B.	105	0.16	68	0.11	87	0.08
L. H.	80	0.17	61	0.12	105	0.10
H. P.	79	0.16	65	0.09	66	0.12
P. H.	88	0.18	68	0.12	72	0.12
N. S.	50	0.16	82	0.11	74	0.12
E. G.	83	0.21	74	0.12		
E. H.	85	0.16 (0.12 to 0.09)§	75	0.12		
A. N.	77	0.18	60	0.15		
*H. H. cycle		0.15 to				
lengths		0.25				
0.64 to						
1.40 second						
Average	80	0.17	68	0.111	88	0.11

*This case is excluded from the averages because of the presence of auricular fibrillation and varying intervals dependent on preceding cycle length.

†The interval in extrasystoles with QRS deflection downward in Lead I and upward in Lead III.

‡The interval in extrasystoles with main QRS complex upward in Lead I and downward in Lead III.

§During the transition from bundle-branch block to normal type of QRS complex, the QRS-carotid interval shortened.

The duration of the interval between the QRS complex and the carotid pulse in premature beats has special interest. In Case H. H. of the group with bundle-branch block in which auricular fibrillation was also present, the intervals in the premature beats with relatively small pulses were greatly prolonged (up to 0.25 second), whereas the beats falling after the longer pauses had an interval of only 0.15 to 0.17 second (Fig. 3A). A small part of the delay in the premature

*Most of these data were included in Table III of the report by Wolferth, Margolies and Bellet.¹ Nichol¹⁸ has recently published similar data on the time relations of the QRS complex of the electrocardiogram and the left subclavian pulse. Although Nichol apparently regards his findings as sufficient for judgment regarding the side of the significant lesion in bundle-branch block, it had not seemed to us safe to do so, even when comparisons with venous pulse tracings were available. Such evidence falls short of proof. It was this conclusion that led us to the attempt to apply the roentgenkymographic method, so that direct measurements of the intervals between the QRS complex and the aortic and pulmonary artery pulses could be made.

beats might be accounted for by lessened pulse wave velocity,* but most of it was probably due to delay in the beginning of ejection. A similar prolongation of the interval was observed in Case M. R. in connection with an extrasystole of supraventricular type (Fig. 3B₂). However, in this same case the intervals in ventricular extrasystoles

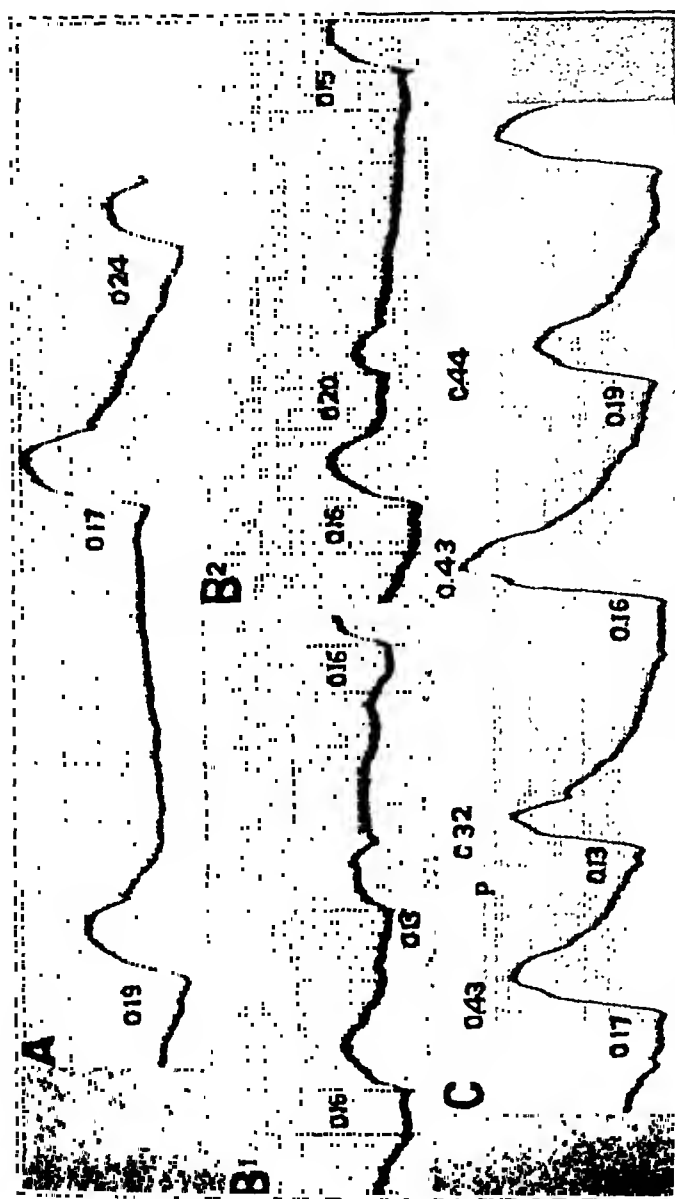


Fig. 3.—Factors influencing the duration of the interval between the beginning of the QRS complex and the upstroke of the carotid pulse in cases with the common type of bundle-branch block. A, Case H. H. (Table II). Auricular fibrillation. The duration of the diastolic period preceding the beat. The interval is longer in the relatively premature beats.

B-1, Case M. R. (Table II). Extrasystoles with main QRS deflections oppositely directed to that of the common type of bundle-branch block. Despite the prematurity of the beats the interval is shorter.

B-2, Case M. R. (Table II). Extrasystoles with main QRS deflections similar to those of the common type of bundle-branch block. The interval is lengthened in the premature beats.

C, Case R. J. (Table II) illustrates the same phenomenon as B-1. The numbers at the top indicate the duration of the interval from the beginning of the QRS complex to the carotid closure (See Fig. 9-A).

with main QRS deflections opposite in direction to those of the rhythmic bundle-branch-block beats were actually shorter than those of the rhythmic beats, despite the possibly lessened velocity of the feeble premature pulse waves (Fig. 3B₁). In Case R. J. a similar shortening of the interval was observed in ventricular extrasystolic beats whose

*R. H. Turner, in the discussion of the presentation "Observations on Arterial Function" (R. H. Turner and W. A. Sedeman) before the American Society for Clinical Investigation, April 30, 1934, stated that the velocity of pulse waves in premature beats differed very little from that of normal beats.

main QRS deflections were opposite in direction to those of the rhythmic beats exhibiting bundle-branch block (Fig. 3C). Wiggers has found that in left ventricular premature systoles the pressure in the left ventricle rises in advance; in right-sided extrasystoles the right ventricular pressure rise precedes. When this state of affairs exists, from 0.03 to 0.06 second may elapse between the contraction of the two ventricles and asynchronous ejection from the two ventricles takes place.¹⁹

These observations made on extrasystolic beats appear to indicate that the delay in ejection from the left ventricle in the common type of bundle-branch block is not due to feebleness of the contractions, but is dependent on some special peculiarity in the spread of the impulse which causes a delay in the response of the left ventricle.

The most striking evidence that delayed ejection from the left ventricle is associated with aberrant spread of impulse was obtained in Case E. H. (Table II and Fig. 4). The transition between the common type of bundle-branch block with QRS complexes having a duration of 0.14 second to QRS complexes having a duration of 0.09 second was

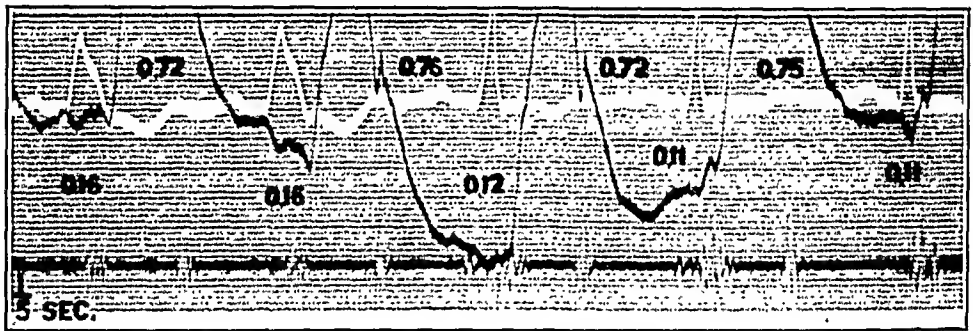


Fig. 4.—Case E. H. (Table II). The effect of transition from the common type of bundle-branch block to normal intraventricular conduction on the interval between the beginning of the QRS complex and the upstroke of the carotid pulse. The interval in the first two beats is 0.16 second, in the third beat 0.12 second, and in the last two beats 0.11 second.

recorded. Coincident with the change in the QRS complexes, the interval between the beginning of the QRS complex and the rise of the carotid pulse changed abruptly from 0.16 to 0.12 and 0.11 second respectively in the two beats following bundle-branch block.

TIME RELATIONS OF THE C-WAVE IN THE VEINS ABOVE THE CLAVICLE

Although the study of the time relations of the carotid pulse demonstrates that ejection from the left ventricle is significantly delayed in the common type of bundle-branch block, it throws no light on the action of the right ventricle. For this reason, the interval between the beginning of the QRS complex and the optically recorded C-wave of the venous pulse just above the right clavicle was measured in a series of 8 cases with the common type of bundle-branch block (7 of which were also included in Table II) and 8 normal controls. The optical apparatus was lined up to avoid parallax. Special care was

taken in the attempt to obtain the venous C-wave (which is most likely dependent on right ventricular activity) and to avoid the arterial C-wave. In the cases having the common type of bundle-branch block, the venous C-wave always fell earlier than the arterial so that the time relations are fairly reliable. In some of the controls, however, there was no certainty that the upstroke of the C-wave was not contributed to or actually caused by the arterial pulse. Nevertheless, the intervals in the cases with bundle-branch block and controls have quite comparable time relations (Table III). It is therefore, justifiable to say that, although in the common type of bundle-branch block the carotid pulse is delayed, the appearance of the venous C-wave in the veins above the right clavicle is not significantly delayed.

TABLE III

TIME INTERVAL FROM BEGINNING OF QRS COMPLEX TO UPSTROKE OF C-WAVE
IN THE VEINS ABOVE THE RIGHT CLAVICLE

THE COMMON TYPE OF BUNDLE-BRANCH BLOCK		CASES WITH NORMAL INTRAVENTRICULAR CONDUCTION	
CASE	TIME INTERVAL (SECOND)	CASE	TIME INTERVAL (SECOND)
R. J.	0.12	W. H.	0.10
M. R.	0.12	M. C.	0.10
R. B.	0.13	A. K.	0.09
L. H.	0.11	J. B.	0.11
E. W.	0.10	E. D.	0.12
H. P.	0.12	P. C.	0.09
P. H.	0.14	A. R.	0.06
H. H.	0.08 to	C. T.	0.15
(Auricular fibrillation)	0.10		
Average	0.116		0.103

While these measurements suggest that in the common type of bundle-branch block ejection from the right ventricle is not delayed, they do not prove the point. The beginning of the venous C-wave does not necessarily bear the same relation to right ventricular ejection as the sharp upstroke of the carotid wave bears to left ventricular ejection. It is quite possible that movement of the heart as a whole may cause a wave to travel up the veins. Furthermore, upward pressure on the tricuspid valve (after closure), which is probably largely responsible for the venous C-wave, may not bear a fixed relationship to ejection. Moreover the velocity of the pulse wave in a low pressure venous system is probably considerably retarded as compared with the velocity in arteries.²⁰

ROENTGENKYMোগRAMS OF THE GREAT VESSELS

The procedure of roentgenkymography to record movements of the heart borders was first attempted by Sabat²¹ and later by Gött and Rosenthal²² in 1912. A method of timing the curves by means of electrocardiograms was first used by Becker²³ in 1914 and later by

Stenström and Westermarck²⁴ in 1926. We have recently published roentgenkymographic tracings of movements of the left auricular border in mitral stenosis.²⁵ The time relations of the roentgenkymograms were analyzed by the use of the superimposed 60 cycle inductive disturbance caused by the x-ray current on the simultaneously recorded electrocardiogram (Fig. 5D).

Roentgenkymography of the great vessels does not, as a rule, yield as satisfactory results as that of the heart, since the contrast with the lung fields is not so sharp. This is particularly true of the pulmonary artery region below the aortic knob, because of the adjacent left hilus shadows, which occasionally made kymography of the pulmonary artery difficult, if not impossible. Roentgenkymograms of the aortic knob pulsations were usually obtained without much difficulty. A slit 1.5 mm. in width was used and the film moved past the slit in a motor-driven cassette carrier. Cassette speeds of 3 to 6 cm. per second appeared to be the most satisfactory. The milliamperage varied from 80 to 100 and the kilovoltage from 80 to 100, depending upon the speed with which the cassette was driven and the thickness of the patient's chest. Only those patients in whom satisfactory records of the aortic knob and pulmonary artery pulsations could be obtained were used. Examples of the best results obtained by this technic are shown in Fig. 5 A, B, and C.

The measurement of the time relations involved several possible sources of error. Since the slit was 1.5 mm. in width, there was bound to be slight haziness in the margin of the photographed waves, although this was minimized by the speed with which the film was moved. There was also a hazy band at the beginning and ending of the kymogram. Measurements were made from the middle of these bands. In most of the faster moving films, the slit image was photographed on the moving film by the rectified full wave 60 cycle current impulses as alternate light and dark bands, which could be used as a time signal, the time between successive dark bands being 1/120 sec. (Fig. 5A). In the other cases, when it was not distinct enough to be so used, the uniformity of speed with which the film traveled had to be tested by measurements of various time intervals on the electrocardiogram and checked against distances traveled by the film. The superimposed 60 cycle inductive disturbance on the electrocardiogram offered a satisfactory time signal for the duration of the roentgen ray exposure. The amplitude of the disturbance in the electrocardiogram was controlled by means of the so-called induction eliminator, the optimum being a band 3 to 5 mm. wide, so as to obtain a readable electrocardiogram (Fig. 5D).

Another factor requiring consideration was the point on the roentgenkymogram marking the arrival of the true arterial pulse wave. In the optically recorded pulse wave there is rarely difficulty in identi-

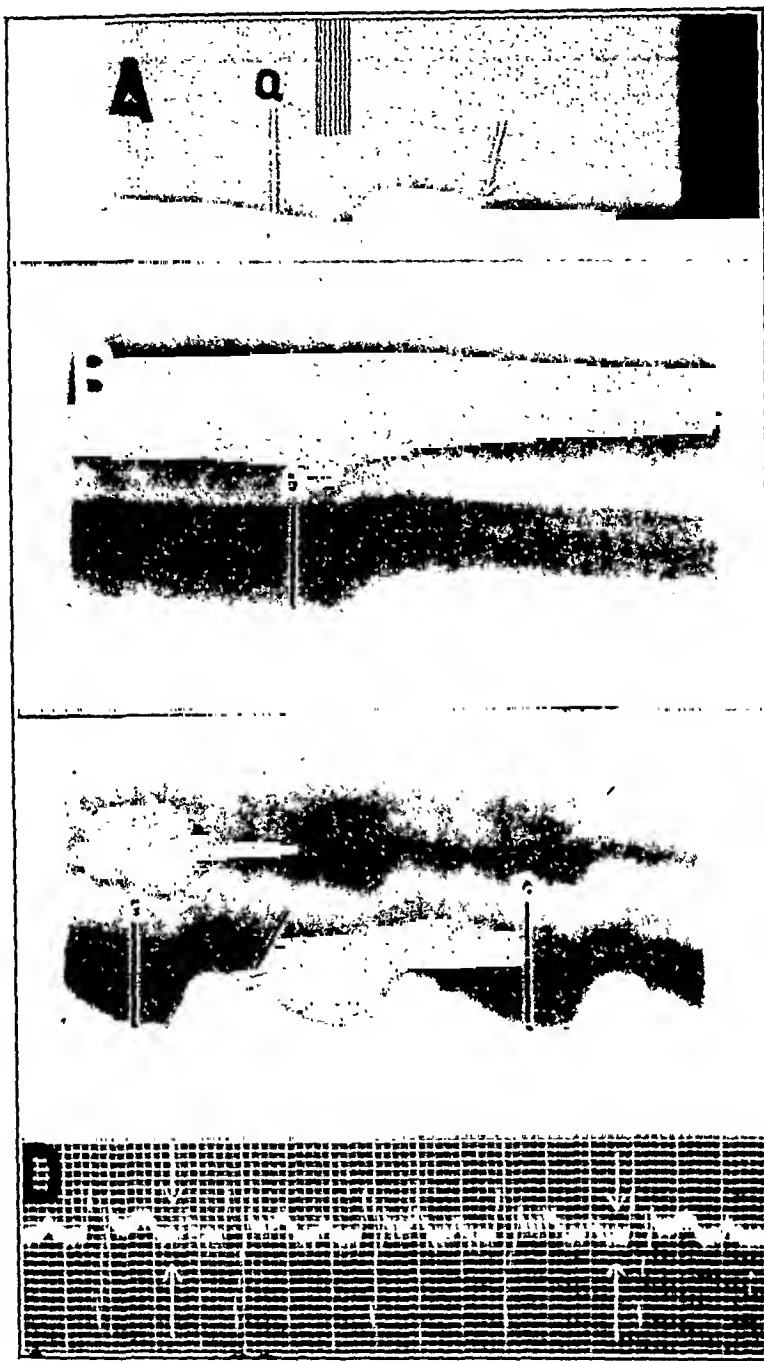


Fig. 5.—Illustration of results obtained in roentgenkymography of the great vessels. The point Q in each roentgenkymogram marks the beginning of the QRS complex.

A, A pulmonary artery pulsation. The incisura is distinctly shown (arrow). The alternate light and dark bands (reinforced in part of the photograph for purposes of reproduction) are due to the effect of the rectified full wave 60 cycle current impulses.

B, An aortic pulse wave. The incisura is not distinct in this case although it is in many aortic pulse waves.

C and D, Simultaneously recorded roentgenkymogram of the pulmonary artery and electrocardiogram (Lead II) of case J. O.C. (Table IV). The pulse is unusually large, probably due to marked arteriosclerosis in the pulmonary vessels. The incisura is well shown (arrow). The transmission of pulsation to adjacent lung structure is considerable. The beginning and the ending of the inductive disturbance in the electrocardiogram are indicated by the arrows.

fying its beginning. The preliminary waves (due probably to auricular systole, movement of the heart during the isometric contraction period and also possibly to movement of the semilunar valve before opening¹⁷) are relatively insignificant, whereas the arrival of the pulse wave initiated by ejection is marked by an abrupt rise in the curve. Although these preliminary movements are rarely recognizable in roentgenkymograms of the great vessels (probably because of their small size), the beginning rise of the pulse wave is usually not so sharply defined as in the magnified curves of the optically recorded waves. In certain cases the possible error in determining the beginning of the pulse is such that the records cannot be used.

The possibility of error due to movement of the vessel as a whole was considered. This movement is doubtless a factor in all roentgenkymograms of the great vessels, particularly of the aortic knob. In certain cases with vigorous heart action, particularly those with aortic insufficiency or hyperthyroidism, the movement of the aorta at the knob may be much greater than just above the valve. We have recorded apparently distorted pulse waves here with a lateral excursion of nearly 2 cm. It seemed, however, that even at the aortic knob, movement of the vessel as a whole did not involve an appreciable error in the time relations. As a matter of fact, the error due to movement of the knob before arrival of the pulse would tend to minimize this evidence of delay in ejection from the left ventricle.

As a result of numerous measurements and controls we have concluded that with satisfactory roentgenkymograms and careful technic there remains a possible error in any individual measurement of 0.02 second. We have attempted to minimize this possible error in determining the intervals between the beginning of the QRS complex and the aortic and pulmonary artery pulse by measuring two or three intervals and taking the average (Table IV). In a few thin-chested individuals with excellent contrast, however, the film was run very rapidly and only a single pulse recorded. In these cases the speed of the film and the presence of the time signal on the film, referred to above, minimized errors in measurement.

It was hoped in the beginning of our work that cases of bundle-branch block would be encountered with either sufficient dilatation of the ascending aorta or tortuosity so that the pulses of the ascending aorta and the pulmonary artery could be recorded in the same film. No such cases were found, and it was, therefore, necessary in all cases to record the aortic pulse at the aortic knob. From available data on pulse wave velocity in large vessels and length of aorta it was estimated that the pulse at the knob should fall 0.010 to 0.015 second later than in the ascending aorta.*

*The point on the ascending aorta from which the length to the aortic knob was measured, was taken at a level comparable to that of the pulmonary artery roentgenkymogram.

TABLE IV

INTERVALS BETWEEN BEGINNING OF QRS COMPLEX AND PULSE WAVES IN AORTA AND PULMONARY ARTERY (AS MEASURED FROM ROENTGENKYMোগRAMS TIMED BY ELECTROCARDIOGRAMS)

CASE	RATE	TO ASCENDING AORTA (SECOND)	TO AORTIC KNOB (SECOND)	TO PULMONARY ARTERY (SECOND)	INTERVAL	INTERVAL
					BETWEEN PULMONIC AND AORTIC PULSE* (SECOND)	BETWEEN 1ST AND 2ND COMPONENT OF SPLIT FIRST SOUND
The common type of bundle-branch block						
W. B.	80		0.15	0.10	+0.04	
R. J.	92		0.15	0.10	+0.04	0.06
M. R.	84		0.17	0.10	+0.06	
R. B.	130		0.17	0.10	+0.06	0.06
L. H.	80		0.22	0.14	+0.07	
H. P.	79		0.16	0.10	+0.05	
Average	91		0.17	0.11	+0.05	
Intraventricular conduction defects and split first sound						
J. O'C.†	98		0.16	0.11	+0.04	0.06
A. O.‡	74		0.12	0.17	-0.05	0.06
J. W.	75		0.14	0.11	+0.02	
E. K.	105		0.08	0.08	-0.01	
J. R.	158		0.08	0.04	+0.03	
C. T.	66		0.14	0.15	-0.02	
G. M.	100	0.12		0.12	0.00	
D. Sh.	115	0.10		0.12	-0.02	
D. Sm.	125		0.09	0.07	+0.01	
W. H.	83		0.15	0.13	+0.01	
Average	103	0.11	0.11	0.10	0.00	
Cases with normal electrocardiogram and split first sound						
L. P.	85		0.13	0.06	+0.06	0.06
S. W.	100		0.12	0.17	-0.06	0.05
N. G.	105	0.07	0.09	0.10	-0.03	0.04
C. S.	120		0.07	0.09	-0.03	0.04
H. B.	92	0.12		0.14	-0.02	0.04
W. H.	94	0.11	0.12	0.14	-0.03	0.05
Average	99	0.10	0.11	0.12		

*The figures in this column give the differences in time between the arrival of the pulse in the ascending aorta and the pulmonary artery, as obtained from the three columns to the left. It is assumed that the pulse wave travels from the ascending aorta to the knob in 0.01 second. This correction is applied in cases of patients whose aortic pulses were photographed at the knob. The plus signs indicate that the pulmonary pulse was the first, and the minus signs that the aortic pulse was first.

†See Fig. 1 B for electrocardiogram.

‡See Fig. 1 C for electrocardiogram.

Measurements of the interval between the beginning of the QRS complex and the beginning of the pulse wave in the aorta and pulmonary artery were obtained in 6 cases with the common type of bundle-branch block and in two cases with conduction defects which did not conform to the common type of bundle-branch block (Fig. 1*B* and *C*). There are also included a series of 8 normal controls with single first sounds and 6 normal controls with split first sounds.

In the normal controls with single first sounds the intervals show considerable variation from case to case. Similar variations were observed in the intervals between the QRS complex and the beginning of the carotid pulse (Table II).^{*} In these controls the apparent asynchronism between the aortic and pulmonic pulse was as great as 0.03 second. No significance, however, is to be ascribed to these variations, since they fall within the range of error of the method, which is not sufficiently accurate to measure such slight asynchronism.

No significant differences in the interval from the beginning of QRS complex to the beginning of the pulmonary artery pulse were found in the cases with the common type of bundle-branch block as compared with normal controls with single first heart sounds. However, in all cases of the common type of bundle-branch block, the intervals between the QRS complex and the aortic pulse showed a significant delay in ejection from the left ventricle. This is evidenced not only by comparison with the controls, but by the fact that in each case of the common type of bundle-branch block the aortic pulse fell much later than the pulmonic. It is of interest that of the two cases mentioned above with intraventricular conduction defect, one had an electrocardiogram differing markedly from the common type of bundle-branch block (Case A.O., Fig. 1*C* and Table IV), and in this case the delay in ejection was on the right side rather than on the left (Table IV).

THE RELATION BETWEEN ASYNCHRONISM IN THE BEGINNING OF EJECTION FROM THE TWO VENTRICLES AND SPLITTING OF THE FIRST HEART SOUND

The time relations of the beginning of the pulses in the aorta and pulmonary artery, as obtained by the roentgenkymographic method, offer an opportunity to test the hypothesis that splitting of the first heart sound is related to asynchronism in certain dynamic events associated with the early phases of contraction of the two ventricles (Table IV).

The time relations of the two components of a split first heart sound to the beginning of left ventricular ejection can be obtained from combined carotid artery and sound tracings recorded without paralax. An allowance of 0.02 second for transmission of the pulse from

^{*}The data suggest that cardiac rate is one of the factors concerned in the duration of the interval; it tends to be shorter in cases with tachycardia.

the aortic valve to the carotid artery is sufficiently accurate for practical purposes. The time relations can also be easily calculated if both electrocardiogram-heart sound and electrocardiogram-carotid artery tracings, made in the same position and with similar heart rates, are available. The most satisfactory method is to record simultaneously without parallax, the electrocardiogram, sound tracing and carotid artery pulse. The only error in this method involves the assumption that the pulse requires 0.02 second to be transmitted from the aortic valve to the carotid artery.

In the measurements, we have disregarded small vibrations of an indeterminate character, probably subsonic, which frequently fall very near the beginning of the QRS complex. Large vibrations of the type which doubtless represent audible sound begin rather abruptly, usually in the range of 0.03 to 0.07 second after the beginning of the QRS complex and sometimes slightly later. That these large vibrations begin before left ventricular ejection can readily be determined by the methods mentioned above.

When the first heart sound is split, the time interval from the beginning of the QRS complex to the first component is about the same as in the case of a single first sound. If a well-damped recording apparatus is used, however, the large vibrations are found to cease abruptly, and a quiet interval is recorded until the second component of split sound occurs. The recorded vibrations of both components may be of approximately the same amplitude or they may be much larger in one component than in the other. A striking characteristic is the short duration of each sound component as compared with the prolongation that is often observed when no splitting of sound can be detected.

An attempt was made to obtain data regarding the relation between the two components of a split first sound and ventricular ejection in two cases with the common type of bundle-branch block,* two cases with other types of bundle-branch defect, and six cases with no delay of intraventricular conduction. In the four cases with conduction defect both optically recorded carotid pulse and roentgenkymographic tracings of the aortic and pulmonary artery pulses were used to determine the times of ventricular ejection. In the six cases without intraventricular conduction defect, roentgenkymographic tracings were used.

The cases with normal intraventricular conduction and split first sounds showed a significant degree of asynchronism between the beginning of right and left ventricular ejection, comparable to that of bundle-branch block and greater than that found in normal controls

*Splitting of the first sound could be detected on auscultation at times in some other cases of bundle-branch block, but because of the feebleness of the sounds could not be satisfactorily recorded. Occasionally only a single faint sound or systolic murmur could be heard and, less frequently, a faint sound and a murmur.

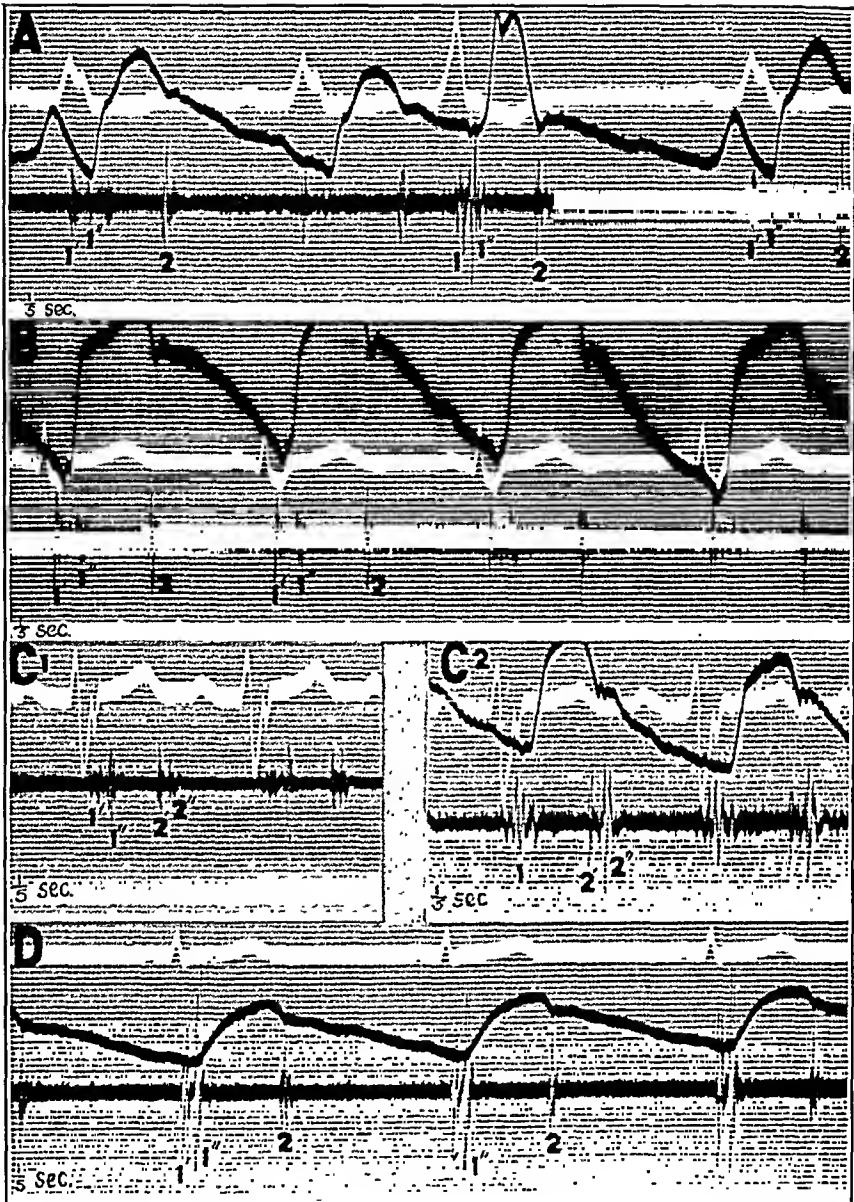


Fig. 6.—The relation of the two components of split first heart sounds to the upstroke of the carotid pulse.

A, Case M. R. (Table IV). The common type of bundle-branch block. The carotid upstroke follows the second component of the split first sound both in the sequential beats and in the ventricular extrasystole.

B, Case A. O. (Table IV). The three leads of this patient's electrocardiogram are shown in Fig. 1 B. Intraventricular conduction defect of a type which is probably right sided. The carotid upstroke follows the first and precedes the second component of the split first sound.

C, Case J. O'C. (Table IV). The three leads of this patient's electrocardiogram are shown in Fig. 1 B. The tracing C-2 was made several months after C-1. In C-1 the first sound is definitely split. In C-2 it is not split but prolonged. The upstroke of the carotid is late in relation to the beginning of the sound suggesting that the left ventricular component is the latter part of the prolonged sound.

D, Normal control with split first sound. In this case the carotid upstroke follows the second component of the split first sound. In certain normals it may follow the first and precede the second component.

(Table IV). However, in 5 of the 6 cases in this group left ventricular ejection preceded the right, and even in the case in which left ventricular ejection followed right ventricular ejection, it did not tend to be so late as in bundle-branch block.

In the two cases with the common type of bundle-branch block, the carotid pulse tracings showed clearly that ejection from the left ventricle did not begin until after completion of the second component of the split first sound (Fig. 6A). In one case (J. O'C, Table IV) with intraventricular conduction defect, a similar relation was observed. However, in the other case with intraventricular conduction defect of a type which we are beginning to believe is due to a lesion in the right branch,* (A.O., Table IV and Fig. 6B) left ventricular ejection preceded the second component of the first sound.

Because of the fact that the roentgenkymograms were made with the patient in the standing position and the sound tracings in the recumbent position, the attempt to correlate the time relations of the sounds and ejection from the two ventricles by this method is subject to possible error. In certain cases splitting of the first sound may be noted in one position or phase of respiration, and not obtained in other positions or other phases of respiration. However, in each case included in this study, the precaution was taken to determine by auscultation that, with the patient in the standing position and holding his breath, splitting of the first sound was present just before and after the roentgenkymograms were made.

The data, as obtained by roentgenkymography, regarding relationships of ventricular ejection from the two ventricles to the two components of split first sounds are presented in Table IV. The relations observed are as follows: (1) Although significant asynchronism in ejection may occur without demonstrable splitting of heart sounds (possibly because of feebleness or inaudibility of one component), it was present in all cases studied with widely split first sounds. (2) The first component of the split first sound invariably precedes ejection from either ventricle. (3) If the split between the two components of sound is wide, ejection from one ventricle (in some cases the right, in others the left) may precede the second component of sound, or the two may be practically synchronous. (4) The second sound component invariably precedes ejection from the later ventricle. (5) The first component of sound precedes ejection from one ventricle by approximately the same interval that the second component precedes ejection from the other ventricle.

Asynchronism in the onset of ejection might be due to (1) asynchronism in the onset of contraction in the two ventricles, (2) differ-

*F. N. Wilson and his coworkers²² have presented evidence, derived from electrocardiograms that record the potential variations produced by the heartbeat at a single point, which supports this view.

ences in duration of the isometric contraction phase in the two ventricles. Both mechanisms may be operative in the same case and may either increase or diminish the degree of asynchronism. Presumably in cases of bundle-branch block asynchronism depends mainly on delay in the onset of contraction in one ventricle, due to delay in the arrival of the excitatory process. However, it does not seem reasonable to suppose that a similar delay may occur when intraventricular conduction is normal. Under such circumstances differences in the isometric contraction phase may occur, possibly due to different dynamic factors in the two ventricles. Failure to consider this possibility has led many observers to the conclusion that asynchronism in contraction is impossible when the electrocardiogram is normal.

According to Wiggers and Dean,²⁷ the main vibrations of the first heart sound coincide with the beginning of the intraventricular pressure rise. While it is certain that the first heart sound is initiated during the isometric contraction phase, and that it is probably due to rapid rise of intraventricular tension, we are not concerned with the actual mechanism of sound production at present. We do wish, however, to emphasize the fact that, when the first sound is split, each component begins before the end of the isometric contraction phase of one ventricle or the other. The asynchronism in sound as well as the onset of ejection is therefore related to asynchronism of some event during the isometric period.

The foregoing observations have certain applications to the consideration of single first heart sounds. It would appear that the important duality is composed of the right and left ventricular components of sound. So-called prolonged or impure first sounds are sometimes, possibly always, due to imperfect synchronism of the right and left ventricular sound components. That this is the case can actually be demonstrated in some cases with phasic splitting of the first sound, in which at some times prolonged first sounds and at other times split sounds may be recorded. Therefore the view not infrequently expressed that prolonged or impure first sounds are to be regarded as evidence of cardiac muscle abnormality should be reconsidered.

Possibly one of the reasons why investigators have made so little progress in determining the mechanism of production of the first heart sound has been failure to take into account the right and left ventricular contributions to the sound. This problem can be simplified, to some extent at least, if the sound production of one ventricle is studied separately from that of the other ventricle. As a matter of fact such a separation is essential if accuracy is to be obtained in recording time relations.

THE RELATION BETWEEN ASYNCHRONISM IN THE END OF EJECTION FROM THE TWO VENTRICLES AND SPLITTING OF THE SECOND SOUND

The end of the ejection phase is marked by the sounds due to closure of the semilunar valves, although as pointed out by Wiggers, actual ejection ceases shortly before valve closure.¹⁷ However, practical



Fig. 7.—The relation of the carotid incisura to split second sounds.

A, Same case as shown in Fig. 6 A. The common type of bundle-branch block. The carotid incisura follows the second component of the split second sound.

B, Same case as shown in Fig. 6 B. Probable right-sided intraventricular conduction defect. The carotid incisura follows the first and precedes the second component of the split second sound.

C, Same case as shown in Fig. 6 C. Intraventricular conduction defect, side of lesion questionable. The carotid incisura follows the first and precedes the second component of the split sound. All the data in this case indicate that pulmonic ejection begins ahead of aortic ejection and ends later.

D, Normal control. The carotid incisura follows the first and precedes the second component of the split second sound. In certain normal controls the carotid incisura may follow the second component.

difficulty is often encountered in the attempt to measure the end of ejection by the second sound, since the sound is frequently split both in normal and in diseased hearts. In bundle-branch block there tends to be unusually wide splitting of the second sound.* In normals, the

*Rarely the second sound in bundle-branch block shows merging of the two components or only slight splitting. In one case in which the latter occurred, the ejection period in the left ventricle, as calculated from the carotid pulse, was unusually short (0.21 sec., Case E. G. Table II).

second sound may be (1) single, (2) split in every beat, or there may be (3) respiratory phasic incidence of splitting.²⁸ Phasic incidence of splitting was not observed in our cases of bundle-branch block.

In view of these facts it seemed advisable to test the hypothesis that splitting of the second sound is due to asynchronism in closure of the aortic and pulmonic valves.

Whenever the second sound is definitely split, the component identified with aortic closure can be determined readily by comparing the time relations of the second sound to the incisura (diastolic notch) of the optically recorded carotid pulse. Since the wave forming the ascending limb of the incisura is reflected as a result of aortic closure, it should reach the carotid artery approximately 0.015 to 0.025 second after aortic closure. Consequently the sound due to aortic closure should precede the bottom of the carotid incisura by approximately this same interval.

TABLE V

TIME INTERVALS IN CASES OF THE COMMON TYPE OF BUNDLE-BRANCH BLOCK BETWEEN EACH COMPONENT OF THE SPLIT SECOND SOUND AND THE INCISURA OF THE RIGHT CAROTID ARTERY PULSE			TIME INTERVALS IN THE COMMON TYPE OF BUNDLE-BRANCH BLOCK BETWEEN EACH COMPONENT OF THE SPLIT SECOND SOUND AND THE BEGINNING OF THE DESCENDING LIMB OF THE JUGULAR V-WAVE		
CASE	1ST COMPONENT (SECOND)	2ND COMPONENT* (SECOND)	CASE	1ST COMPONENT† (SECOND)	2ND COMPONENT (SECOND)
H. P.	0.07	0.02	H. P.	0.08	0.04
R. J.	0.10	0.01	M. R.	0.08	0.02
M. R.	0.06	0.01	L. H.	0.11	0.04
L. H.	0.07	0.01	R. B.	0.12	0.06
R. B.	0.07	0.02	W. W.	0.08	0.03
E. G.	0.08	0.02			
H. H.	0.04 to 0.06	0.01 to 0.02			

*The time relations of the second component indicate that it represents aortic closure in all cases studied.

†The interval between pulmonic closure and the beginning descent of the V-wave measures approximately the duration of the isometric relaxation phase of the right ventricle. The normal range is 0.06 to 0.13 second. Therefore, in Cases H. P., M. R., L. H. and W. W., the first component must represent pulmonic closure. In Case R. B. the second component was found by its relation to the carotid incisura to represent aortic closure. Thus it would appear that in this case also the first component represents pulmonic closure.

Observations were made in 7 cases with the common type of bundle-branch block possessing split second sounds (Table V and Fig. 7A). In all of the 7 cases, the incisura bore a significant time relation to the second component of the split second sound and never to the first component. Similar studies have been made in other types of cases having split second sounds (with and without intraventricular conduction defect, Fig. 7 B, C. and D). In these cases, in contrast with the findings in the common type of bundle-branch block, aortic closure is frequently identified with the first component of the split sound.

The method used for attempting to identify pulmonic closure depends on the duration of the isometric relaxation phase as measured

from the second heart sound to the beginning of descent of the V-wave in the optically recorded pulse from the veins just above the right clavicle. Wiggers¹⁷ states that the isometric relaxation phase can be determined by measuring the interval between the bottom of the incisura of arterial pulse and the beginning of the V-wave drop in the venous pulse in the neck. Since the first depends on left ventricular and the second on right ventricular action the interval between them

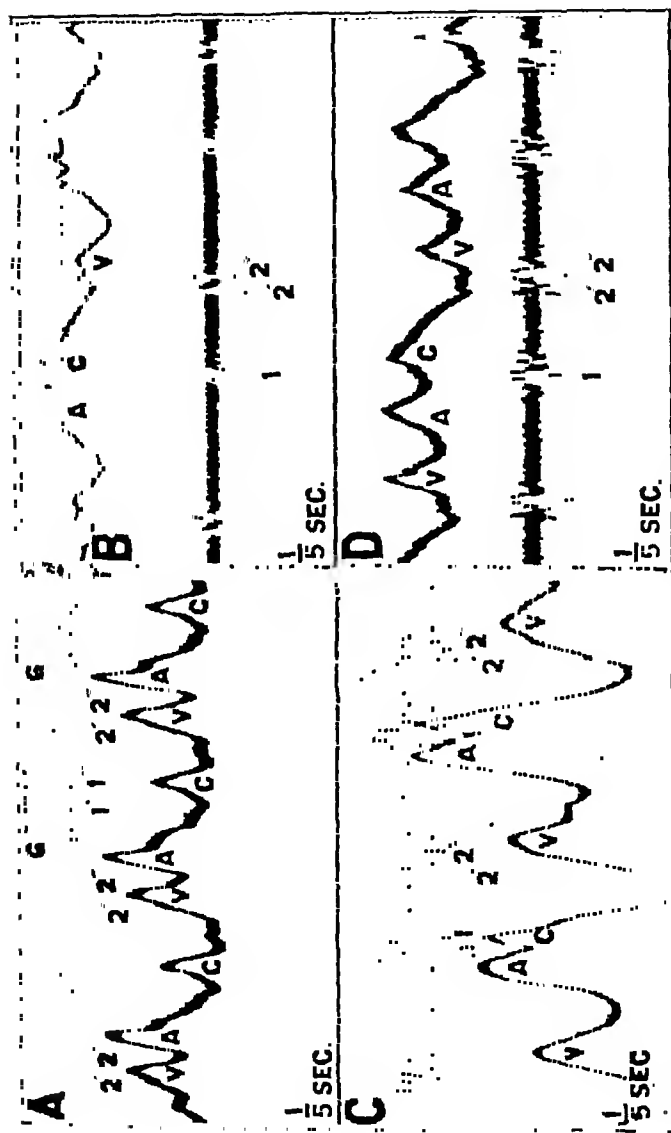


Fig. 8.—The relation of the V-wave of the jugular pulse to the components of split second sounds. The duration of the isometric relaxation phase is in the range of 0.06 to 0.13 second at ordinary heart rates. Thus pulmonic closure should precede the beginning descent of the V-wave in the same range.

A, The common type of bundle-branch block. The beginning descent of the V-wave bears a significant relation to the first (and not to the second) component of the split second sound. B, Normal control. Same case as shown in Fig. 7 D. The descent of the V-wave falls 0.11 second after the first and 0.06 second after the second component of the split second sound. Therefore, the method is of no value in this case in determining pulmonic closure. The time relations to the carotid incisura indicated that the first component was aortic. Presumably, therefore, the second component is pulmonic.

C, Same case as shown in Fig. 7 B. D is same case as in Fig. 7 C. In both cases the descent of the V-wave bears a significant relation to the second component of the split second sound and not to the first component. The second component in both cases, therefore, must represent pulmonic closure. In Fig. 7 it was shown in both cases that the relation of the second sounds to the carotid incisura indicated that the first component represented aortic closure.

may be regarded as an index of the isometric relaxation phase *only* when aortic and pulmonic closure are synchronous. Since Katz¹⁵ has shown that these events are usually asynchronous in dogs, and the frequency of split second sounds suggests that they are often asynchronous in human beings, the accuracy of the method used by Wiggers is not established except for cases with single second sounds.

In a previous report²⁵ we presented data on the duration of the isometric relaxation phase as measured from the second heart sound

(1) to the beginning descent of the V-wave and (2) to the opening snap in mitral stenosis. It was found that cardiac rate is a factor in the duration of the isometric relaxation phase. At ordinary heart rates, the duration of this phase tended to fall in the range of 0.07 to 0.12 second with outside limits of 0.06 to 0.13 second. In the presence of extreme tachycardia, the interval may be as short as 0.04 second and in marked bradycardia as long as 0.19 second. Another fact which emerged from that study was that when the second heart sound is single, in cases of mitral stenosis with the opening snap, the beginning descent of the V-wave (which marks the end of the isometric relaxation phase of the right ventricle) tends to fall at the same instant as the snap (which marks the end of the isometric relaxation phase in the left ventricle). However, when the second sound is definitely split, the descent of the V-wave begins either before or after

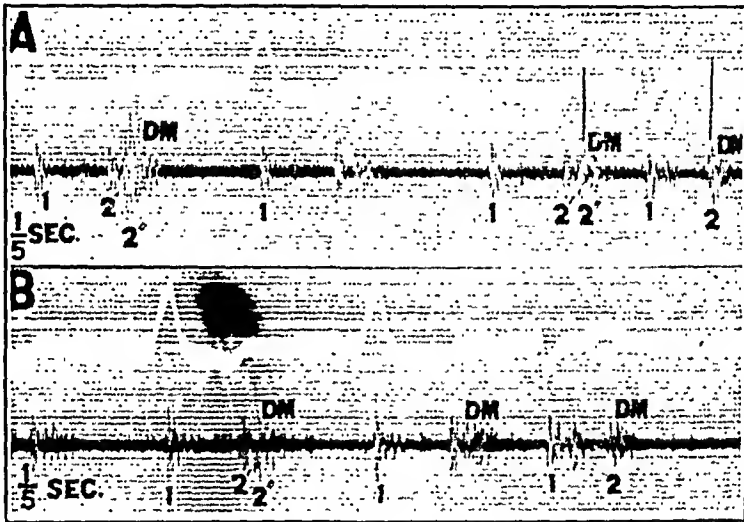


Fig. 9.—Case R. J. (Tables II and IV, also Fig. 3 C). The relationship of the diastolic murmur of aortic regurgitation to the second heart sound in the common type of bundle-branch block. The murmur is continuous with the second component except in extrasystoles with the main QRS complex oppositely directed to the rhythmic beats. In the extrasystoles the murmur is continuous with the beginning of the second sound. The time of the carotid incisura (obtained from Fig. 3 C) is shown on the last two beats of the top strip. This point should follow the beginning of aortic regurgitation by approximately 0.02 second.

the opening snap, indicating that under these circumstances, the isometric relaxation period does not tend to end synchronously in the two ventricles.

The time relations of the V-wave in the optically recorded pulse of the veins just above the clavicle were compared with the two components of the split second sound in the common type of bundle-branch block in 5 cases (Table V). In each case, the interval between the first component of the split second sound and the descent of the V-wave falls within the customary range found when the second sound is single. In 4 of the 5 cases the interval from the second component of the second sound was shorter than that of isometric relaxation

phases recorded at comparable heart rates (Fig. 8), and in the fifth case (R. B.) both components of the second sound fell within the significant range (0.06 and 0.12 second).

From these data the following may be said regarding the common type of bundle-branch block: when splitting of the second sound is recorded, the first component is due to pulmonic closure and the second component to aortic closure. Therefore, ejection from the right ventricle ends earlier than that from the left ventricle. According to the intervals recorded between the two components of the second sound

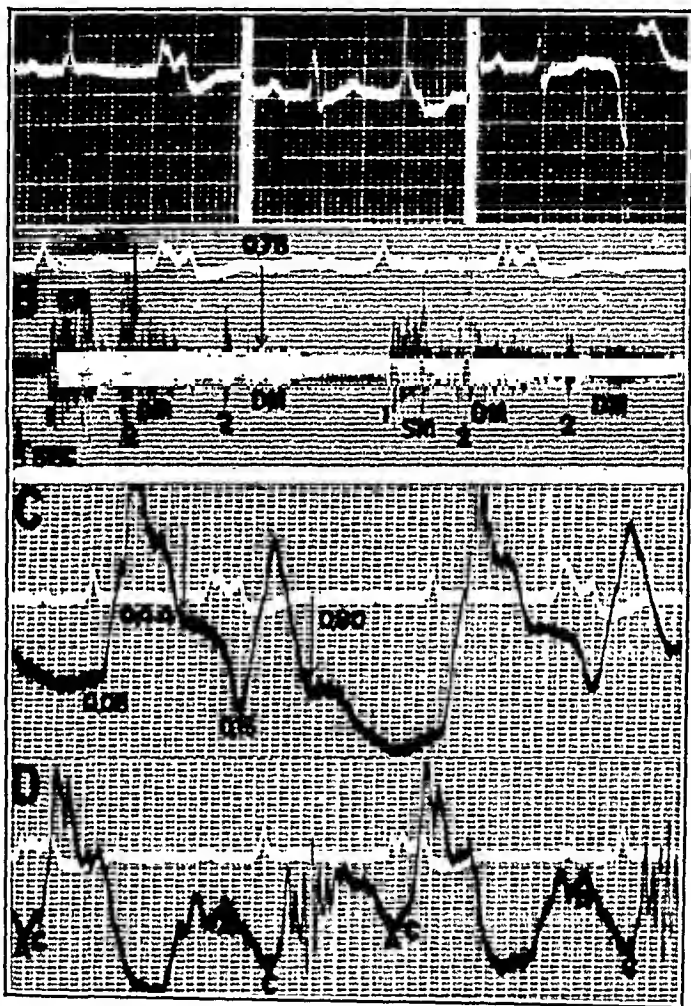


Fig. 10.—A patient with aortic regurgitation and ventricular extrasystoles with main QRS deflections upward in Lead I and downward in Lead III.

A, Electrocardiographic Leads I, II and III.

B, Lead I and sound tracing. In the normal beats no gap is recorded between the second sound (2) and the diastolic murmur (DM), but in the extrasystolic beats a wide gap is present (0.08 second).

C, Lead I and carotid artery tracing. The interval between the beginning of the QRS complex and the upstroke of the carotid is 0.08 second in normal beats and 0.16 second in extrasystolic beats. There is no definite incisura due to the free aortic regurgitation, its position being marked by sudden angulation in the wave (arrows). This point which should follow the beginning of aortic regurgitation by approximately 0.02 second has been marked off (arrows) on the sound tracing in B.

D, Lead I and jugular pulse tracing. There is apparently no delay in the venous C-wave in extrasystolic beats comparable to that of the carotid wave. The actual measurement is somewhat obscured by the presence of an A-wave.

in our cases, ejection ended on the right side from 0.03 to 0.09 second before it ended on the left. The conclusion that in the common type of bundle-branch block, aortic closure tends to follow pulmonic closure may be further tested by studying cases with valvular lesions which produce murmurs or sounds having a definite relationship to aortic closure.

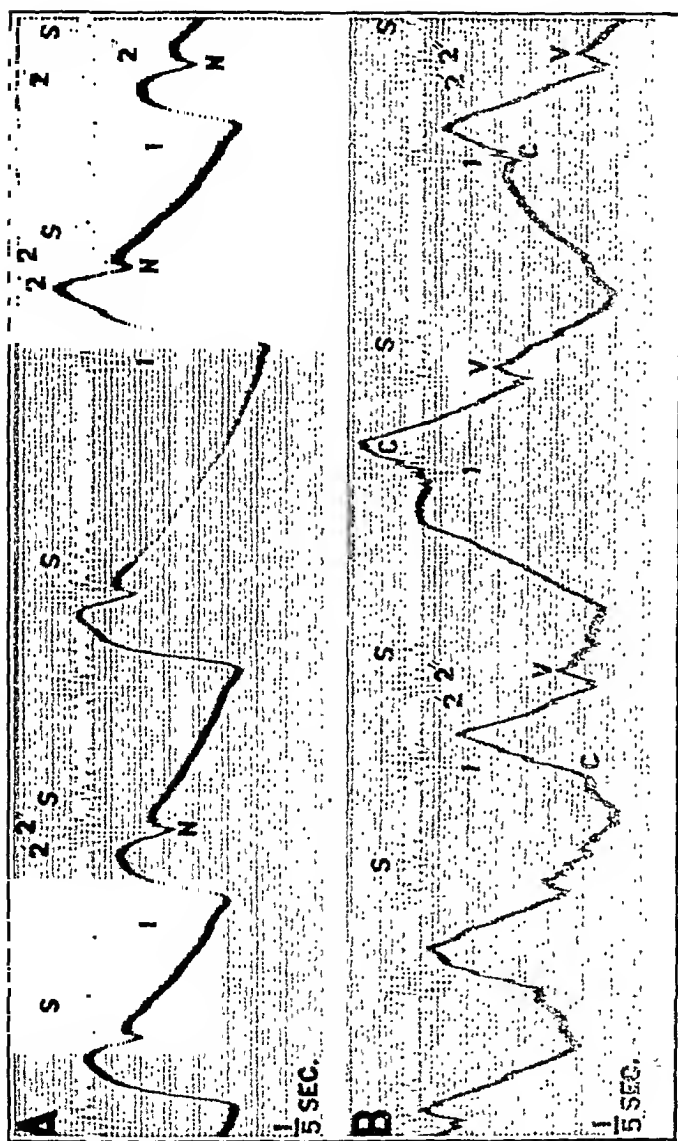


Fig. 11.—Case H. H. (Table II and Fig. 2 C and Fig. 3 A). Exhibiting the common type of bundle-branch block, auricular fibrillation, a split second sound, and the opening snap of mitral stenosis.

A. Sound (recorded by the electrocardiographic string) and carotid artery tracing. The carotid incisura (n) identifies the second component of the second sound as being due to aortic closure. The time relations of the opening snap (s) to the two components also indicate that the second component must be aortic closure (time to opening snap 0.10 second), since the interval between the first component and the snap is too long for a significant relationship (0.16 second).

B. Sound and jugular pulse tracing. The time relations of the beginning descent of the V-wave to the second sound (0.11 second between first component and V-wave drop) indicate that the first component must be pulmonic closure. Thus three separate procedures for identifying components of split second sounds (time relations to carotid incisura, descent of V-wave, and the opening snap) give concordant results. Furthermore, the beginning descent of the V-wave (which marks the end of the isometric relaxation phase in the right ventricle) precedes the opening snap (which marks the end of the isometric relaxation phase in the left ventricle) by approximately 0.06 second. The asynchronism in this case is due mainly to the fact that the isometric relaxation phase begins earlier in the right ventricle and ends earlier, rather than to unequal duration in the two ventricles.

We have had the opportunity to make fairly complete studies in one case with the common type of bundle-branch block and well-developed aortic insufficiency (Case R. J., Tables II and IV). It is well known that the murmur of aortic insufficiency is either practically continuous with or replaces the aortic second sound. It was noted in this case, both by auscultation and by sound tracings (Fig. 9), that the diastolic murmur was continuous with the second component of the split second sound. However, when ventricular extrasystoles with

the main QRS deflection downward in Lead I occurred, the murmur was continuous with the first component. These findings indicate that in the beats exhibiting the common type of bundle-branch block, the second component of the split second sound was identified with aortic closure.

Studies of a similar nature were made in a patient exhibiting aortic insufficiency, intraventricular conduction time within normal limits in sequential beats, and occasional ventricular extrasystoles with QRS complexes, upward in Lead I, and downward in Lead III, somewhat resembling although not identical with those found in the common type of bundle-branch block (Fig. 10A). It was found in the sequential beats that the carotid pulse and the C-wave obtained over the right jugular vein began 0.08 second after the initial wave of the QRS complex (Fig. 10 C and D). Sound tracings showed that the diastolic murmur due to aortic insufficiency was practically continuous with the second heart sound in the sequential beats (Fig. 10B). In the extrasystolic beats, however, the carotid pulse was delayed, beginning 0.16 second after the initial wave of the QRS complex (Fig. 10C), although the venous C-wave maintained the same time relations of 0.08 second to the QRS complex as it did in sequential beats (Fig. 10D). Furthermore, in the premature beats the diastolic murmur did not follow immediately after the second sound but there was a gap between them of 0.09 second. It would therefore appear that in these extrasystolic beats the delay was limited to the left side and that the extrasystoles must have originated in the right ventricle.

In mitral stenosis the opening snap is associated with the attempt of the crippled mitral valve to open.²⁵ It is therefore closely related in time to the end of the isometric relaxation phase of the left ventricle. It bears a definite time relation, in any given case, to aortic closure, being uninfluenced by relative shifts in the position of pulmonary closure. Thus, the component of a split second sound which represents aortic closure can be identified in certain cases of mitral stenosis by this time relation, as well as by the incisura of the carotid pulse. In our one case of mitral stenosis with the common type of bundle-branch block, both methods showed that the second component of the split second sound was aortic (Fig. 11). In one case with ventricular extrasystoles having complexes homologous to those of the common type of bundle-branch block, aortic closure in the extrasystolic beats was represented by the second component of the split second sound.^{25*} In another case with extrasystoles of the opposite type, aortic closure in the extrasystolic beats was represented by the first component of the split second sound.^{25†}

*Fig. 6, Strip 1-A in reference 25.

†Fig. 6, Strip 3 in reference 25.

In control cases with widely split second sounds, whether or not intraventricular conduction defect be present, the time relations between the two components of the second sound and the beginning descent of the V-wave show that in some of these cases, in contrast to the findings in the common type of bundle-branch block, the second component represents pulmonic closure (Fig. 8B).

SUMMARY

Graphic studies of comparable time relations of certain events associated with the heartbeat in the common type of bundle-branch block and various types of control cases reveal the following:

1. A systolic bifid apex impulse can be recorded in some, but not in all, cases of bundle-branch block. It may also occur in cases without bundle-branch block. These facts should be considered in assessing the diagnostic value of the systolic bifid apex impulse and indicate that it cannot be regarded as reliable evidence of the presence of bundle-branch block.

2. Comparison of the interval between the beginning of the QRS complex and the beginning of the carotid pulse wave in cases with bundle-branch block, in normal controls, and in cases with cardiac decompensation, indicates that ejection from the left ventricle is significantly delayed in the common type of bundle-branch block. No comparable delay is observed in cases of cardiac decompensation without intraventricular conduction defect. Evidence is presented to establish the fact that the delay is associated with the particular type of aberrant spread of the excitatory process which occurs in the common type of bundle-branch block.

3. Comparison of the intervals between the beginning of the QRS complex and the beginning of the C-wave recorded from the veins immediately above the right clavicle in cases of the common type of bundle-branch block and normal controls shows no significant delay in bundle-branch block. This finding suggests, although it does not definitely prove, that in the common type of bundle-branch block there is no significant delay in the contraction of the right ventricle.

4. Roentgenkymographic tracings of the aorta and pulmonary artery were made in 6 cases with the common type of bundle-branch block, 2 cases with other types of intraventricular conduction defect and split first sounds, 8 normal controls with single first sounds, and 6 cases with split first heart sound, but without intraventricular conduction defect. The time relations of the aortic and pulmonary artery pulses were compared. The results were as follows: (a) In the common type of bundle-branch block, the interval between the beginning of the QRS complex and the beginning of the aortic pulse was significantly prolonged in each case. (b) In the normal controls with

single first sounds the differences in time between the beginning of the aortic and pulmonary artery pulses fell within the limits of error of the method. (c) In the cases with split first sounds, both with and without intraventricular conduction defects, the differences in time between the beginning of the aortic and pulmonary artery pulses tended to be greater than in the control cases with single first sounds. In 2 cases the differences were as great as those observed in bundle-branch block. However, in one of these two cases the aortic pulse preceded the pulmonic; whereas in all cases of the common type of bundle-branch block, the pulmonary artery pulse preceded the aortic.

5. All the findings support the hypothesis that in the common type of bundle-branch block there is asynchronism in the beginning of ejection from the two ventricles due to delay on the left side. The evidence also indicates that in some, possibly all, cases with split first sounds but without intraventricular conduction defect, there is asynchronism in the beginning of ejection from the two ventricles.

6. The association between asynchronism in the beginning of ejection from the two ventricles and splitting of the first heart sound; the correspondence in the intervals between the two components of the sounds and the degree of asynchronism; and the relationship of the arterial pulse to one or the other component indicate that (1) the split first sound has a right ventricular and a left ventricular component, and that (2) separation of these components is due to asynchronism in certain of the early phases of cardiac contraction in the two ventricles.

7. Splitting of the second heart sound can be heard on auscultation and recorded in most cases with bundle-branch block. It is also frequently present in cases without evidence of cardiovascular damage.

8. It can be proved by the following methods for identifying aortic and pulmonic closure that splitting of the second heart sounds is due to asynchronism in closure of the two semilunar valves. (a) When the second heart sound is split, the component associated with aortic closure can be identified by its time relation to the incisura of the carotid artery pulse. (b) When the sound is *widely* split, the component associated with pulmonic closure can be identified by its time relations to the beginning of the descent of the V-wave recorded from the veins above the clavicle. (c) When either the diastolic murmur of aortic insufficiency or the opening snap of mitral stenosis is present, additional methods for confirming the identity of the components of the second sound may be available.

9. In the common type of bundle-branch block, pulmonic closure usually precedes aortic closure. Occasionally they may be practically synchronous.

10. In cases with split second sounds but without intraventricular conduction defect, either aortic or pulmonic closure may come first.

11. All the evidence obtained in this study is in accord with the hypothesis that the common type of bundle-branch block is due to delay in spread of the impulse on the left side. The view held by Eppinger and Rothberger, and Lewis is no longer tenable. No support was obtained for the statement that it is unjustifiable to attempt to localize the side of bundle-branch block from the direction of the major initial complex in the three limb leads of the electrocardiogram.

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A NEW METHOD FOR THE RECORDING OF HEART SOUNDS*

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SINCE heart-sound registration has thus far failed to correspond with auscultatory findings, most clinicians have taken little interest in these investigations. Clinical cardiology is based primarily upon the response of the human ear, and the various methods of recording heart sounds do not correspond to the obvious auditory impression. Thus, one often reads reports of heart-sound registration in which the author states that a particular recorded sound is inaudible. The purpose of this study has been to introduce distortion so as to duplicate mechanically the failings of the human ear. Another difficulty in reading the graphs so far reported, resides in the impossibility of determining when a sound begins or ends, for the base line merges into the sound, which presents no sharp and easily recognizable distinction. Such records, therefore, do not fulfill their primary purpose, which is the exact timing of the heart.

It would be possible to construct a system of cardiology based upon the findings of the type of mechanical registration which we have just discussed. Such a system, however, would bear no relation to clinical cardiology as it is practiced today. We trust that the following report will show that heart-sound registration can be made to correlate with clinical findings, and can be employed readily and with as much ease as electrocardiographic study for the elucidation of cardiac pathology.

THEORETICAL

There are numerous methods available for the recording of sound in general and of heart sounds in particular. The features common to all such methods are (1) a receiver for the sound and (2) a recorder which registers, usually by optical methods, the motion of some part of the recording apparatus. These devices have been constructed so as to make the motion of the recorder or, more strictly, the recording light-beam an exact reproduction, on an enlarged scale, of the motion of the diaphragm or other suitable part of the receiver. It was found early in the history of heart-sound registration that many murmurs could be recorded more clearly if distortion were introduced into the system in such a direction as to stress higher frequencies. The scale of enlargement was made to vary with the frequency of the sound in such a way that higher frequencies were enlarged to a greater extent

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than lower frequencies. Distortion is also found to be necessary if the apical impulse, which is a strong mechanical vibration, but entirely inaudible, is not to appear in the record.

Detailed analysis of the many previous methods of introducing distortion is unnecessary. Suffice it to indicate that they were usually of a haphazard nature, sometimes consisting of the introduction of a sidearm opening in a recording capsule, at other times of the use of a transformer or condenser in an electrical recording system. But, to our knowledge, there has never been any quantitative requirement set on this distortion.

It is the aim of this work to set up definite requirements for this frequency distortion. We require that the sound record be one readily

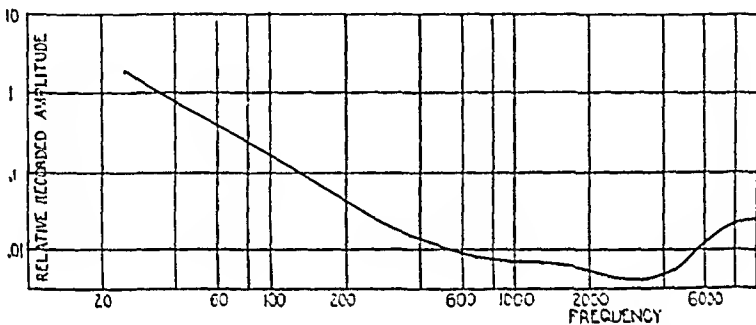


Fig. 1.—The amplitude recorded by a sound pressure recorder of uniform frequency response to sounds of various frequency of the same loudness level (30 D B., A.I.E.E. Standard) *Electrical Engineering*, November, 1933, 52-11-p. 745.

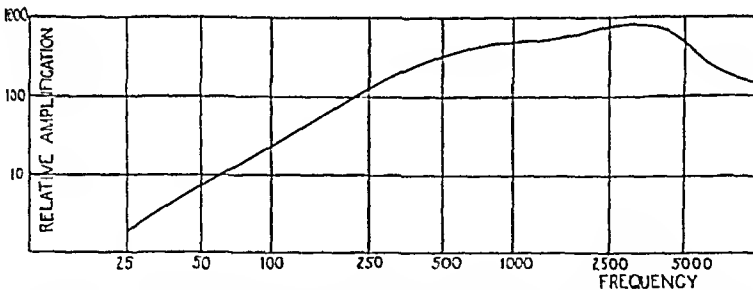


Fig. 2.—Relative amplification required at various frequencies so that sound pressure records yield equal amplitudes for equal loudness level (30 D B) at all frequencies.

interpretable in terms of the sounds heard by the ear, in order that the mass of clinical experience in auscultation may be applied without difficulty to a heart-sound record. Our criteria must depend upon the typical response of a normal ear. Fig. 1 shows the amplitude of deflection which would be registered by a distortionless sound pressure recorder responding to pure notes of low intensity and of the same loudness, as judged by the average ear. It is evident that our requirement may now be put into exact quantitative terms. Distortion must be so introduced that the amplitudes of deflection for various frequencies are equal for the same loudness. The distortion must therefore be of the type shown in Fig. 2. There should be no recorded

amplitude for vibrations of any magnitude of frequency outside audible limits and the magnifications must increase strongly with increased frequency up to about 3000 cycles, and then decrease to the upper limit of audibility. As a practical matter we may neglect all frequencies above 1000. First, there are practically no important heart sounds of dominant frequencies above this point; and second, the speed of the film necessary to record higher frequencies would produce a record of unwieldy length.

We have constructed a recorder in fair approximation to these principles. It consists of (1) an electromagnetic receiver which is strapped to the patient, (2) a high gain amplifier in which, by appropriate choice of circuit constants, the necessary distortion is introduced, and (3) an electromagnetic oscillograph throwing a moving light-beam into the camera slit of an electrocardiograph, also connected to the patient. Because of difficulties which we hope to remove in the future it has been impossible to introduce quite as much distortion as is theoretically required, but our existing apparatus represents a reasonable approach to the ideal.

In viewing the records, another factor of great importance must be considered. The ear, like other sense organs, is characterized by a logarithmic response. That is to say, sounds differing by equal sensation differences, possess amplitudes differing not by a constant amount but by a constant factor. For example, if four sounds differ by equal sensation level differences and the recorded amplitudes of the first and second are respectively one and two millimeters, then the third and fourth will be represented by amplitudes of four and eight millimeters respectively. Consequently, records represent relative loudness of different sounds only in a very qualitative way. These deviations from what might be termed a true auditory record are inherent in all the methods of recording and cannot be obviated by any pure frequency distortion. There is, however, a way of overcoming these difficulties by means of a method which we expect to report in the future.

In spite of all the deviations of the present system from the ideal, the improvement upon all other methods is marked. We do not record the inaudible low frequency vibrations so evident in the records of other experimenters. We have had no case of recorded sounds which on careful auscultation could not be heard, and we have recorded all audible sounds. Our records have this in common with any system, that they enable much more accurate conclusions, based on timing, to be drawn than the unaided sense organs permit.

PROCEDURE

This method of heart sound registration is extremely simple. All that is required is a stationary set-up which is more or less perma-

nently adjusted, and a quiet room. The microphone is strapped to the patient's chest. He is instructed to hold his breath during the recording, which takes fifteen to thirty seconds. The entire procedure consumes no more than five minutes and is performed with no discomfort to the patient. The apparatus is not fragile and easily permits one to take eight or nine records in an hour.

Base Line.—The ideal base line would be a solid streak without vibrations which would facilitate enormously the legibility of sound registration. Apparently, this is extremely difficult to obtain in an electrical circuit with the high amplification required. It will be noted that our records show a base line consisting of a uniform frequency and amplitude. With practice in reading, one is soon able to observe the slightest irregularity in this line. Hence, the beginning of the heart sounds can be timed with precision. The instant of change from

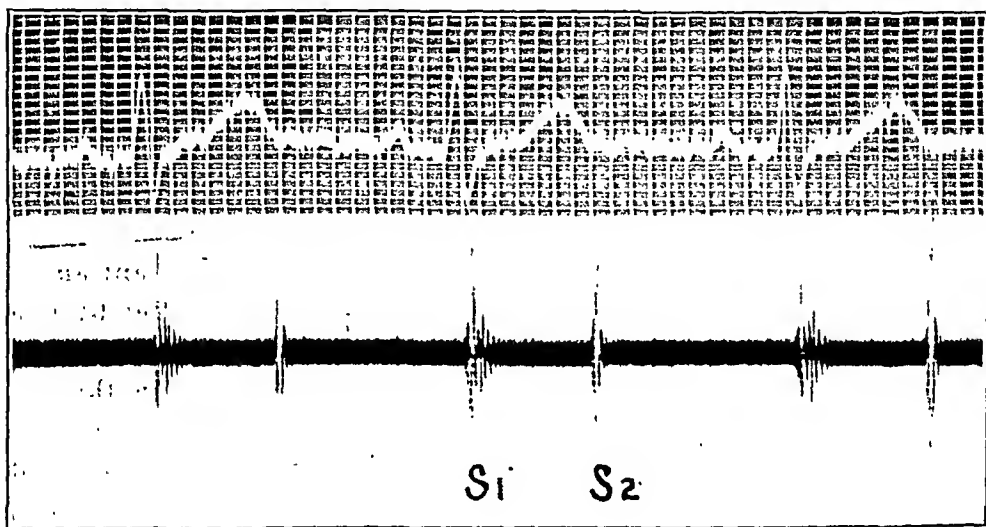


Fig. 3.—Male, twenty-six years old, normal heart. Sounds at apex. Serrated first sound and second sound. No murmurs. Record S_1 begins on terminal portion of down stroke of R-wave, duration $4/50$ sec. Begins with two low amplitude vibrations, followed by higher amplitude, higher frequency element, ends with gradual decrescendo of lower frequency.

S_2 begins at end of down stroke of T-wave, duration $2/50$ sec. Begins with moderate amplitude and high frequency, followed by higher amplitude and higher frequency element, ends with fast decrescendo of lower frequency.

S_1 , first sound at apex; S_2 , second sound at apex.

NOTE: The "serrated" first sound is caused by the marked changes in frequency.

the base line is independent of the recording amplification used, although naturally the larger the amplification the more obvious the change.

Artefacts.—Numerous artefacts will appear in records. They are determinable largely by their irregular distribution and lack of rhythm. They are produced in the following ways: (1) breathing of the patient (the patient is cautioned to hold his breath while the film is running); (2) tension of the chest and muscles (if the patient does not hold his body in relaxation, irregular sounds are produced); (3) extraneous sounds (the extreme sensitivity of the mechanism re-

sponds to all sorts of noises in the environment such as vibration of the building, distant noise, borborygmus, etc.).

CHARACTERISTICS OF THE FIRST AND SECOND HEART SOUNDS

Time.—In these records the first heart sound begins simultaneously with the down stroke of the R-wave of the electrocardiogram. It never begins sooner than the apex of the R-wave.* Hence, any sound registered before the apex of the R-wave would be diastolic in time. The second sound occurs simultaneously with the second half of the down stroke of the T-wave.

Duration.—In our series, the first sound varies between 0.04 and 0.12 second. Any sound longer than 0.12 second includes a murmur. The second sound lasts 0.04 to 0.06 second.

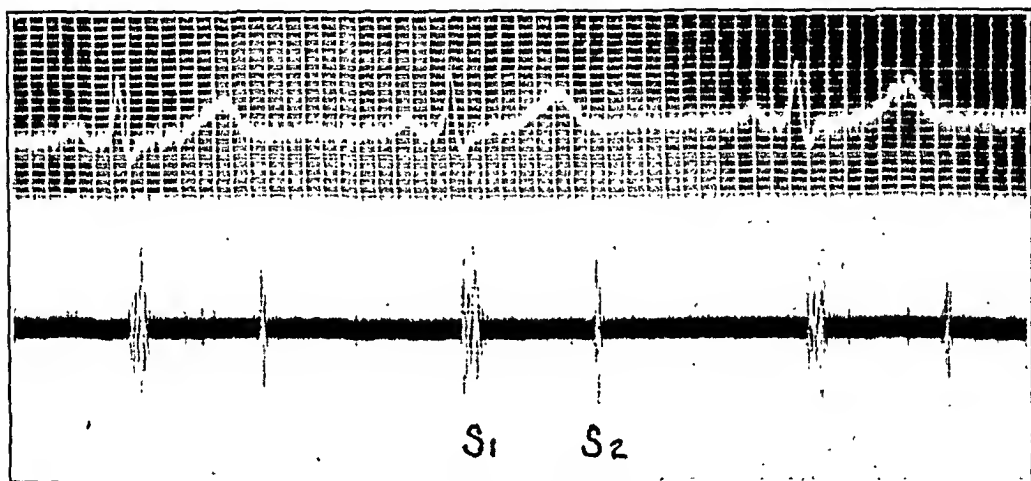


Fig. 4.—Male, thirteen years old. Catarrhal Jaundice. Normal Heart. At apex are heard a split first sound and a second sound. No murmurs.

Record S_1 begins at lower third of down stroke of R-wave, duration $4/50$ sec. S_1 begins abruptly with high amplitude and high frequency, is definitely split, the second part of the split sound being of higher amplitude, ends with a decrescendo of lower frequency and amplitude.

S_2 begins at the end of the down stroke of the T-wave, duration $2/50$ sec. Begins abruptly with high frequency and high amplitude, ends with a slight decrescendo.

S_1 , first sound at apex; S_2 second sound at apex.

Frequency.—The frequencies of the sounds are mixed. By means of a measuring microscope we have been able to determine the frequency of each oscillation of the graph. We find a large range of frequencies, and are reporting only the dominant ranges in this paper. The dominant frequencies range between 50 and 300 cycles a second. The first sound generally shows one to three low amplitude, low frequency vibrations (about 50 per second), followed by a higher amplitude, higher frequency component (100 to 300), which is in turn followed by a decrescendo usually of lower frequency than the major com-

*We have no explanation for the apparent significance of the apex of the R-wave; however we have found no exception to this rule even in cases of widened QRS complexes.

ponent. This last corresponds with the auscultatory finding, for generally the first heart sound has a clearly decreasing ending. The second heart sound generally starts abruptly with high amplitude and without preliminary low amplitude components. Most frequently it ends abruptly as it has begun, though occasionally there is a decreasing finish.

Figs 3, 4, and 5 illustrate the various points.

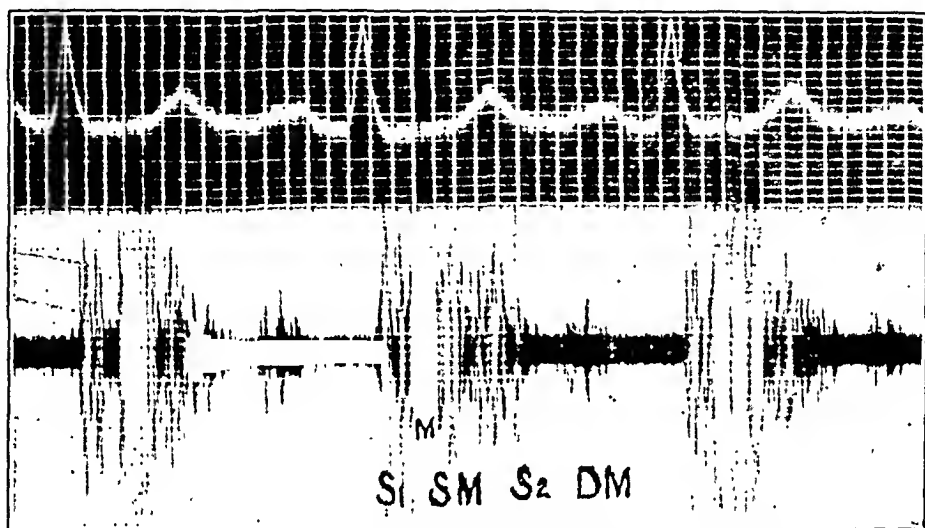


Fig. 5.—Male, thirteen years old, with active rheumatic fever. Over apex is heard a long systolic murmur in which the first sound cannot be distinguished. Part of systole is occupied by a loud musical murmur. The systolic murmur is continuous with the second sound, and after a short diastolic interval a diastolic murmur is heard. There is no presystolic element to the diastolic murmur.

Record S_1 begins on the down stroke of the R-wave, and is continuous with a long systolic murmur occupying all of systole. This in turn is continuous with the second sound. Then there is a noiseless interval for $2/50$ sec. followed by a diastolic murmur lasting $5/50$ sec. Presystole is free of sound.

NOTE: A musical murmur of very high frequency and amplitude occupies part of systole.

S_1 , first sound at apex; SM, systolic murmur; M, musical murmur; S_2 , second sound at apex; DM, diastolic murmur.

SUMMARY

We have presented a new type of recording apparatus which possesses distortion simulating that of the human ear. This permits strict correlation between clinical cardiology and phonocardiographic records. In addition we have established an even base line which permits accurate timing of the beginning and end of heart sounds. The fundamental characteristics of the first and second sounds are described.

We suggest that further phonocardiographic studies be performed along these lines. This may be expected to yield more fruitful results than has hitherto been possible.*

Our thanks are due to Dr. Marcus A. Rothschild, without whose enthusiasm and assistance this study could not have been undertaken.

*Since offering this paper for publication, our attention has been called to the work of Posener and Trendelenburg (Ztschr. f. Kreislaufforsch. 21: 15, 1929) who employed a principle quite similar to that offered here. To our knowledge they have not described their technic in detail.

THE COURSE OF RHEUMATIC HEART DISEASE IN ADULTS*†‡

I. FACTORS PERTAINING TO AGE AT INITIAL INFECTION, THE DEVELOPMENT OF CARDIAC INSUFFICIENCY, DURATION OF LIFE AND CAUSE OF DEATH

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A FOREWORD to these reports of Dr. DeGraff and Miss Lingg would scarcely be necessary were it not that consciously in their investigation a method of analysis was utilized, the power of which for their purpose is sometimes not fully realized. Though a foreword is perhaps unnecessary, there are implications in their study to which attention may, nevertheless, be profitably directed. A method is wanted in analyzing events in the course of long-drawn-out diseases which is not essential in studying the brief illnesses of infectious origin, to which attention has been so predominantly directed these two or three generations past. The association of lesion with structural defect, of form with function, is readily established in diseases of brief duration. The changes in the lungs in the course of lobar pneumonia, at least in their superficial aspects, are well known, though many problems no doubt remain to be solved. These diseases are attended furthermore by so many unequivocal signs and symptoms as to render relatively simple and transparent their dependence on the temporary alterations in structure which underlie them. How to arrive at an understanding of average behavior is, moreover, more or less appreciated by those who have concerned themselves with the effort to estimate the significance of these correlations and have attempted to weigh the influence of therapeutic agents on the course of these diseases. All this is, relatively speaking, simple; what are generally regarded as phenomena relevant to an illness occur so quickly that to witness the events of an infectious disease from its beginning to its end is a common experience to many observers.

The situation in the case of chronic diseases, which should in many cases no doubt be designated preferably diseases of long duration, is

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very different. Rheumatic disease of the heart is such a one. It is not often the opportunity of individual physicians to follow cases of this sort from onset to termination. Yet for many reasons, to do so is indispensable if knowledge of several sorts is to become available. That this disease is one, extending from what is frequently its stormy febrile beginning to an end having little apparent formal relation to it, required the observation of many decades to suggest. The fact seems now firmly established that there is a form of cardiac disease of which individuals die many years after the original rheumatic affection which occasioned it has completely disappeared. But what is scarcely understood is the fate of individuals in the intervening period and how long this period endures. Studies like this by Dr. DeGraff and Miss Lingg are, to all intents and purposes, pioneer works in elucidating the facts. In order that the facts should emerge, it was necessary to apply to them carefully defined terms, bearing on a variety of phases of this ailment. Once awareness was established of the phenomena which require recognition so as to measure the course of events unequivocally, clarity began to dawn. The duration of the various phases of rheumatic cardiac disease is becoming known. For this purpose the value of mathematical analysis has been learned. The error is often made that, in this connection, the use of statistical methods is an end in itself. Nothing can be further from the facts. Actually, the method is merely an instrument employed in the interests of description of the natural phenomena. But as an instrument it is invaluable, as these studies, and so many others in widely different fields of inquiry, amply demonstrate.

If it were not important to learn the history of this disease and of its various stages, first on its own account and second in order to judge of the health of patients and their ability in each of them, it would become of prime importance, nevertheless, to acquire this information in order to appraise the success of therapeutic procedures. Whoever has had experience in making such estimations knows the numerous logical difficulties involved in arriving at conclusions, even in simple situations. When the difficulties multiply, as they do in the case of diseases naturally of long duration, the complexity of analysis obviously increases. In any therapeutic enterprise in such situations almost the first question that requires answer concerns the influence of agent or procedure on *duration*, either of the disease as a whole or of any one of its phases. It makes a difference, furthermore, in which phase therapeutic interference is attempted. A second almost equally important question relates to the effect on the state of the patient's *health* in any one of the several phases of their illness. It is not a matter of indifference whether it is in the first or the last phase of so complicated a process in which a remedy is applied. It may matter,

furthermore, whether a consequence of instituting a procedure, an operation to excise the thyroid gland, for example, is a relief of disability or one which, although it does so, hastens on meanwhile the moment of the inevitable end. Other things being altogether equal, patients will wish perhaps to choose which is a preferable course for them.

The results of the present studies and of other similar ones which show so clearly the course of events in rheumatic cardiac disease and define so precisely the duration of each of its phases must, it seems, form the basis hereafter in appraising the success of any influence which is brought to bear upon it with the view to its modification. That the observation of many cases, each exactly studied, is necessary and the whole procedure of analysis difficult and time consuming is merely to state an inescapable fact; in no other way, in all likelihood, are convincing answers to be secured to problems which require urgently to be solved.

I

TO DESCRIBE rheumatic fever, especially its cardiac phase, is difficult because of its long duration. No one sees its beginning, middle, and end. Since the process of the disease is continuously active, an anatomical evolution takes place which it is extraordinarily difficult to reconstruct. To obtain a complete description, evidence of its various stages must be assembled piecemeal.

The problems presented by the extremely variable manifestations of rheumatic infection, particularly cardiac, make it necessary to study this disease from several points of view. Only by following this course can a proper description of its natural history, extending as it does over many years, be secured. The description must be based on three types of analysis.

First, its onset must be exactly known, and for this reason the types of initial infection, their incidence, their severity and certain other attributes, supplemented by bacteriological and immunological studies, must be described.

Second, the lesions must be described. These can now be identified. With this knowledge and the evidence from case histories, it may be possible to reconstruct the anatomical course of disease; though an account of the intermediate stages cannot escape being uncertain and fragmentary.

Third, patients must be observed throughout the course of the disease. To be successful the observations must be recorded so that they can be properly analyzed. Accurate description of this sort is the contribution which the Heart Committee of the New York Tuberculosis

and Health Association¹ is attempting to make. Since the facts dealing with the initial lesions and with the histological changes cannot always be secured, it has seemed advisable to lay emphasis on describing, as well as this can be done, the course of the disease.

For completeness of description all three methods are necessary. The use of the first facilitates recognition of the disease; the second establishes its anatomical criteria; and the third forecasts its course.

THE SAMPLE

A study of 1,633 cases of rheumatic heart disease was made.* The patients included were observed during the ten-year period 1921-1931. At the end of that time 644 (39.4 per cent) had died, 609 (37.3 per cent) were still living, and 380 (23.2 per cent) could not be traced. An analysis of the histories of the 644 dead has been completed and is now presented.

In a study of this nature success depends, as has been said, on the continuous observation of a large group of patients over a period of years. Loss of the records of many patients destroys the value of the sample remaining. The small group remaining is not necessarily representative of the total one. Failure to observe this simple principle is responsible for serious defects found in medical literature.†

The attempt was made to obtain after-histories of patients who could not be kept under continuous observation.‡ Many were traced and many were reexamined. Of others, interval histories and records of intercurrent illness and of treatment administered elsewhere were obtained in the uniform records kept in the heart clinics of New York City.¹ Many were traced through death certificates filed with the Bureau of Records of the Department of Health.§ By all these means, in the total group of 1,633 patients the fate of 73.3 per cent was learned; 80.7 per cent of those in the clinic, 71.3 per cent in the hospital ward, and 66.6 per cent of the private patients.

Those patients who were victims of a rheumatic infection but not subsequently of cardiac involvement are not included. Coombs² pointed out that 25 per cent of his rheumatic patients apparently recovered completely and showed later no clinical evidence of heart disease. Morse³ found an even higher percentage (37 per cent).

The etiology was recorded as "unknown" in 193 (30 per cent), but mitral stenosis developed, nevertheless. Examinations post-mortem as well as clinical observations suggest that the etiology was rheumatic, though the initial infection must have been so slight as to have passed unnoticed. There is little evidence to support the view that mitral stenosis in the younger age groups can occur otherwise than in rheumatic infection. These patients are therefore included in this study.

*The basic facts are derived from observations of patients in the adult cardiac clinic of Bellevue Hospital, the Third Medical Division of Bellevue Hospital and from private practices, recorded in a uniform manner on the charts provided by the Heart Committee of the New York Tuberculosis and Health Association, or, rarely, on the progress sheets of Bellevue Hospital. The practices of Dr. John Wyckoff and of Dr. Arthur C. DeGraff have been utilized for this purpose. We are indebted to Dr. Wyckoff for the use of many records and for his supervision of our analyses in many cases.

†For the opportunity of continuous observation of patients we are indebted to the social service staff of Bellevue Hospital.

‡For success in this effort we thank workers assigned to us by the Emergency Unemployment Relief Bureau.

§We are indebted to the Department of Health of New York, N. Y., for permission to make searches through death certificates.

Sex.—Among adult patients different observers report a slight predominance of males in rheumatic heart disease; but if children are studied, the ratio of females to males is reported as about 2 to 1 (Table I).^{2, 4} The reason for the higher in-

TABLE I

SEX

	MALES	FEMALES
DeGraff and Lingg (adults)	55.8%	44.2%
Davis and Weiss ¹² (adults)	56.6%	43.4%
Cabot ⁷ (adults)	52.4%	47.6%
Coombs ² (adults and children)	34.1%	65.9%
Wilson, Lingg and Croxford ⁴ (children)	38.8%	61.2%

idence of females in a group of children than in an adult group is partly explained later when the age at initial infection is discussed.

Incidence of Other Etiological Forms of Heart Disease Complicating Rheumatic Heart Disease.—In 94.5 per cent heart disease was purely rheumatic. In 2.7 per cent the rheumatic lesion was complicated by the presence of either arteriosclerosis or hypertension, or both. In only 6 instances was rheumatic heart disease complicated by cardiovascular syphilis. All of these presented, in addition to disease of the mitral valve, aortitis or aortic insufficiency with a history of lues, or both.

Since patients with rheumatic heart disease die young, cardiovascular syphilis or the so-called senescent forms of heart disease rarely complicate these cases. In fact, most patients afflicted with rheumatic heart disease die before they reach the age at which the other two diseases are usually recognized. No cases of congenital heart disease appeared, chiefly because of the fact that this study deals with an adult group.

THE INITIAL INFECTION

Of chief importance is knowing the date of the initial rheumatic infection. The particular form of onset is not significant, but the lesion was defined strictly in conformity with the criteria published by the Heart Committee.⁵ When there was doubt, the etiology was classified as *unknown*. It is probable that in some cases the *initial infection* represented reinfection, that the actual initial infection occurred earlier but was slight and escaped notice, as when discovery of heart disease antedated the recognition of the initial infection. The date of the first rheumatic manifestation is, however, the only landmark now available in describing the onset of rheumatic disease.

Age.—The range of the ages at which the first rheumatic manifestation occurred was wide, and spread from two to sixty-three years (Fig. 1*). The greatest incidence occurred in the decade from 10 to 19 years (39.6 per cent). The position of the *mode* at age 11 is particularly striking since the *mean* age is 17 years. In order to bring it to 17 years the initial manifestation occurred well beyond age 20

*Figs. 1, 2, 3, 4, 5, and 11 include only those cases in which the date of the first manifestation of infection was known.

in some patients. Eighty-four and seven-tenths per cent were infected before age 30 and only 4.4 per cent after 40 years. Obviously rheumatic infection is a disease of youth. Although a number of patients contracted heart disease in childhood, the series does not include those who died before they were old enough to appear in an adult clinic, usually 14 years. This must also be the case in the series reported by Grant,⁶ in which analysis of the published case histories revealed a mean age at 18 and a mode at 10 years. By not including children who die before they are fifteen the mean age given for the occurrence of the initial infection is higher than it would be if all age groups were represented. Conversely, it is lower when the sample excludes patients whose initial infection occurs after age 14. This is the case in the

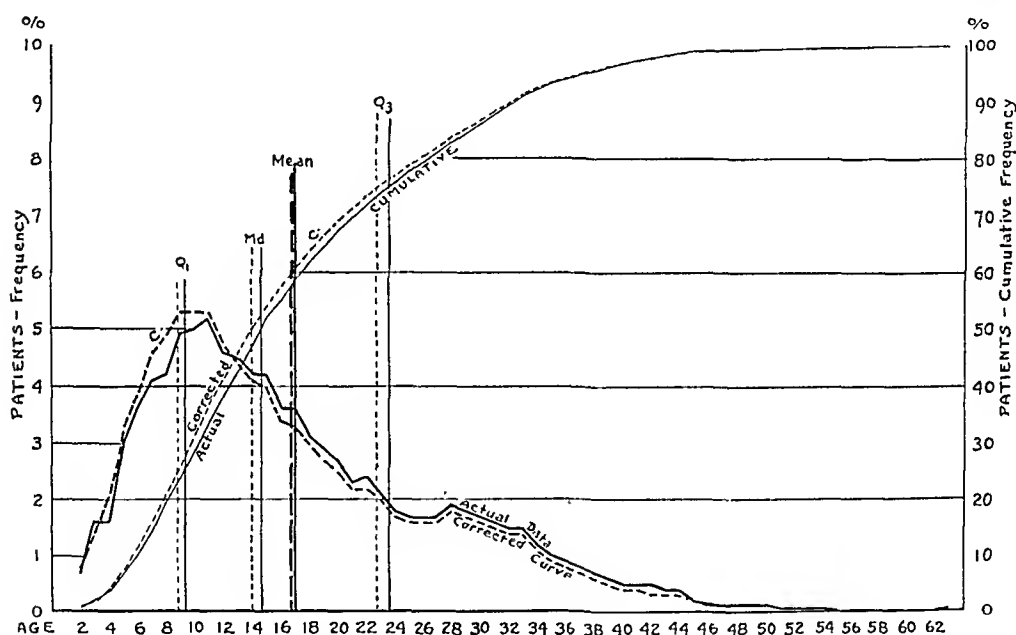


Fig. 1.—Age at first manifestation of infection.

The curves in this and most of the subsequent figures were smoothed by the method of moving averages and the statistical values read from the smoothed curves.

report published by Wilson, Lingg and Croxford,⁴ who give a mean of 8 years. In order to arrive at a true mean, an estimate was made of patients who were excluded from this sample because they died before age 15.* The result places the median at 14 years (Fig. 1 C). The mean at 16.8 is only slightly lower than in the original curve,

*For this purpose Dr. Irving R. Roth was kind enough to allow us the use of data that he has collected in 598 cases of rheumatic infection in children at Mount Sinai Hospital, New York. An estimate of the number of cases lacking because of death before the age for admission to an adult clinic was made by using the following relationship, $A:C::B:X$, when A is the age of the Mount Sinai patients alive after age 14; B is the age of our series less those dead before age 15; C is the age of the Mount Sinai patients dead before age 15; and X is the calculated age of patients who would have been included in our series had they not died before reaching the age of 15 years.

The value of X was determined for each age from 1 to 14. The data were added to the original distribution. The new curve (Fig. 1 C) now includes patients who, it is estimated, died before reaching the fifteenth year.

but the *mode* is flatter and falls earlier, at 9, 10 and 11 years, closer to that of 8 years reported by Wilson, Lingg and Croxford.⁴ The chances of developing initial rheumatic infection are greatest in the age group 9 to 11 and decrease yearly after that. At the same time the *mean* age at onset of rheumatic infection is not so early in childhood as many pediatricians have supposed. It appears that, when a group is not confined to children, about 30 per cent develop their first infection beyond the adolescent period.

Sex.—The age at onset differs in the sexes. To about age 13 years girls predominate over boys. From 13 to 28 years the incidence is about the same for both. Afterward men are more likely to develop rheumatic infection leading to heart disease (Fig. 2). This may explain the higher ratio of females among children, and of males among

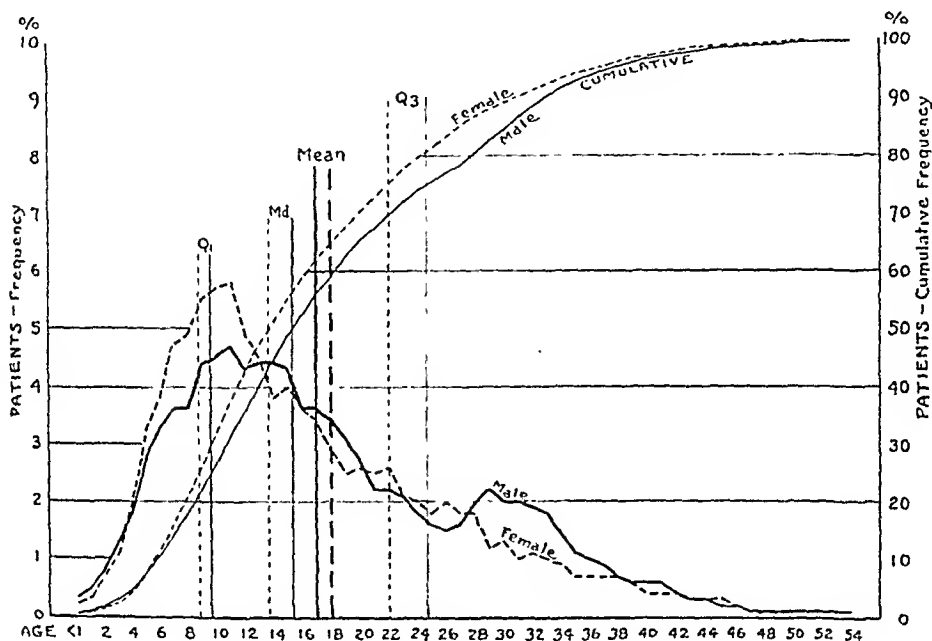


Fig. 2.—Age at first manifestation of infection by sex.

adults referred to above. It may also explain Cabot's⁷ statement that the disease seems to begin earlier in males, since his data represent chiefly older patients.

DURATION OF DISEASE

The virulence of the infection and the degree of myocardial damage produced are extremely important factors in the duration of the disease. Whether such factors can be measured is questionable. It is a common belief, for instance, that repeated attacks of rheumatic fever lead to earlier fatality. Yet Willius⁸ and, recently, Friedberg and Tartakower⁹ found that there is no constant relation between the number of attacks of rheumatic fever and the time when death occurs. An attempt to find such a relation was abandoned when no absolute

criteria for rheumatic activity could be established, nor could the degree of activity be classified. Even if these factors could be correctly appraised, it is only over long periods of time in a home or in a hospital that the desired information could be obtained. These factors then, although important, must be left out of consideration.

The mean duration of life, from the onset of rheumatic infection to death, was found to be 15 years. Although some patients lived much longer, one as long as 58 years, such experiences are rare; 75 per cent lived for less than 23 years after onset (Fig. 3). It may be said, then, that a patient has only an even chance of living 12 years, and only one chance in five of living as long as 25 years after initial infection.

The mean duration of life in this series is very much shorter than the 30 years estimated by Coombs.² He analyzed two groups. His

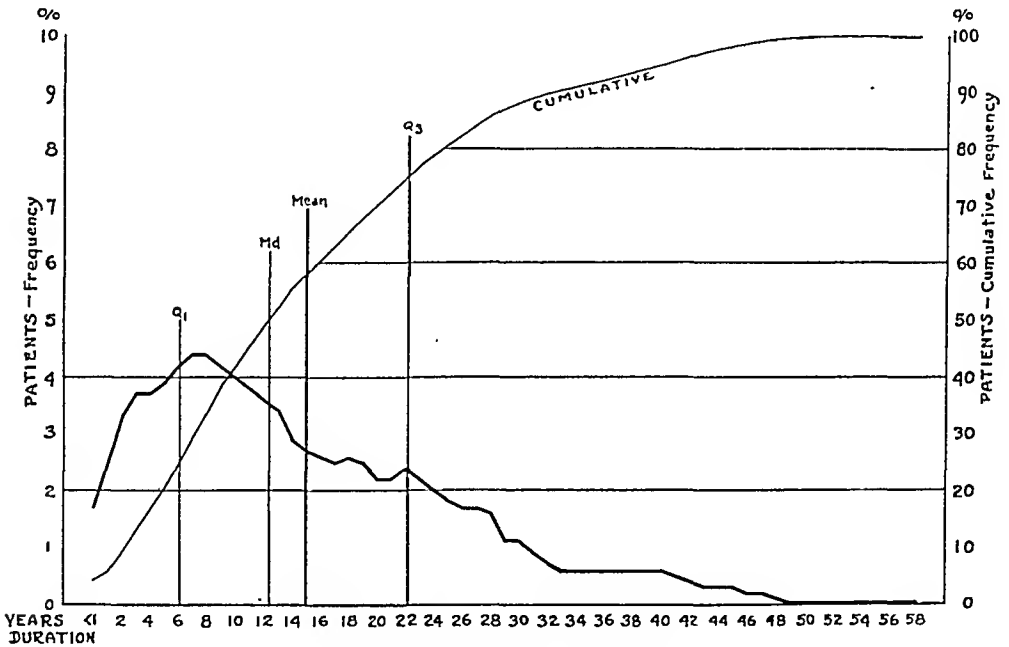


Fig 3.—Duration of disease.

first comprised patients seen very close to the date of onset and followed to an average age of about 25 years; the second, those who presented heart disease when they first came under observation and who had reached at that time an average age of 25 years. By linking the first group to the second he estimated the duration of life to be 30 years. It is obvious that such methods and conclusions are unsound. Willius,⁸ using much the same technic as is used in this report, with a similarly constituted sample, arrived at a mean duration of life of 14 years, which compares well with 15 years in the series here presented.

Grant,⁶ although he says that "it is apparent from this study that the outlook for patients suffering from valve defect is not so bad as

it is generally thought," states that "within 10 years, 473 or about half the cases have died." A word should, perhaps, be said concerning Grant's method of analysis, since without pointing out the differences between his and our presentation, reference to his conclusions in comparison with those presented in this report may lead to misunderstanding and confusion.

In the first place, Grant's sample consists of 1,000 ex-service men. It is limited to the male sex; it is limited to individuals at or above the recruiting age, and therefore, like our sample, excludes those patients with rheumatic heart disease that do not survive to adult life. It excludes also those who may have been rejected for military service because of cardiac damage, the degree and its definition varying during the course of the war; being limited to *ex-service* men (none came under observation until 1919 when the war was over), it excludes men who may have been recruited in spite of damaged hearts, and yet may not have outlived the strain of military service. The sample, then, is not representative of rheumatic heart disease among males, as a whole; it is not representative even of adult males but is limited to the better risks in the class selected for study. One should expect naturally, therefore, to find in this group of patients a more favorable prognosis than is usual in this disease.

In the second place, he relates prognosis not to any definite event in the course of the disease, but rather to the time when patients happened to come under his observation. This time, quite obviously, does not represent the same stage in the course of the disease in all patients. Statements made in his conclusions, such as, "Fifty-one per cent are known to be alive"; "Forty-seven per cent are known to have died"; or "Auricular fibrillation, present originally in ten per cent, develops later in eight per cent," have, therefore, little bearing, being related in his treatment of the problem to the time of *his* contact with the cases, on the calculation of prognosis.

In the third place, he states his conclusions in terms of valvular disease as a whole, in spite of the fact that this includes two entirely distinct processes of disease, rheumatic as well as syphilitic. His statement that "in a fair sample of the adult male population of the country . . . we see that aortic regurgitation is more common than mitral stenosis and that of all the valve defects syphilitic aortic regurgitation is the most frequent" is not in accordance with reported experience in this country, in which even among adult males rheumatic valvular disease is more common than syphilitic aortic insufficiency. Grant classifies cases of mitral stenosis with or without aortic regurgitation, in the absence of a definite history of rheumatic fever, in a separate rubric "indefinite etiology," even though he believes these cases to be rheumatic. If his table is rearranged and these cases

are included in the rheumatic rubric, it is mitral stenosis which stands out as a more frequent lesion than syphilitic aortic regurgitation.

In studying prognosis Grant divides his cases according to etiology and, furthermore, according to various valvular lesions or combinations of lesions. This method reduces the groups to such small numbers that an estimation of prognosis becomes difficult. There is, however, another difficulty; it is desirable to know the difference in prognosis between syphilitic and rheumatic heart disease without regard to which valve is involved. This analysis Grant has not made. Since he has published summaries of his case histories, we have been enabled to retabulate his data in order to make them comparable to those now presented. Subsequent references to Grant in this paper are based, for the most part, on our own analyses of his data. These reveal, among his deceased rheumatic patients, a mean duration of life of 19 years. Seventy-five per cent lived for less than 26 years. This somewhat longer duration of life than was experienced by the group now studied may be explained by the method of selection of his patients to which reference has already been made.

A similar explanation may be applied to the results published by Friedberg and Tartakower.⁹ They give as a mean duration of life 23 years after first infection in one group (63 cases) and 38 years in another group (29 cases) of patients that presented rheumatic heart disease both clinically and at autopsy. These groups include no patients who contracted the disease before puberty, and the second group comprised not only particularly long lived individuals, but also patients whose heart disease was discovered accidentally, who at no time experienced symptoms of cardiac insufficiency. Unfortunately they did not publish the age distribution of these two groups of patients at the time they first observed them. If, as is implied, they were beyond 30 years of age at that time, so that patients who succumb to the disease before that age are excluded, a mean duration of disease would occur among them that is much longer than would be the case if the sample were not so biased. The fact that the number of cases in these groups is so small and that the mean age at death is as high as 41.8 years, leads to the belief that our deduction is correct. In the series here presented, for example, 46 patients lived for 30 or more years after onset of infection (Fig. 3). If we computed the mean duration of disease in this group, it would exceed 30 years.

The age at the time of initial infection has an important bearing on the duration of life. In general, the younger the patient at first infection, the longer is the interval before death (Fig. 4). This corroborates the experience reported by Willius⁸ and by Friedberg and Tartakower.⁹ It is contrary to the experience of pediatricians⁴ who report an unfavorable prognosis among children when the disease

starts early. Such cases are, however, not included in this sample. In view of these observations, inferences as to prognosis must not be drawn without considering the fact that with advancing age life expectancy decreases even among normal individuals. This was also pointed out by Friedberg and Tartakower.⁹

According to Cabot⁷ the duration of rheumatic heart disease is shorter in men than in women. In this series, as also in the two groups studied by Friedberg and Tartakower,⁹ there is, however, no difference. The curves can almost be superimposed.* For males, the mean duration is 14.9 years, for females 15.0 years; the median is at 12 years and the first quartile at 6 years for both sexes, and the third quartile at 22 years for males and between 20 and 21 years for females.

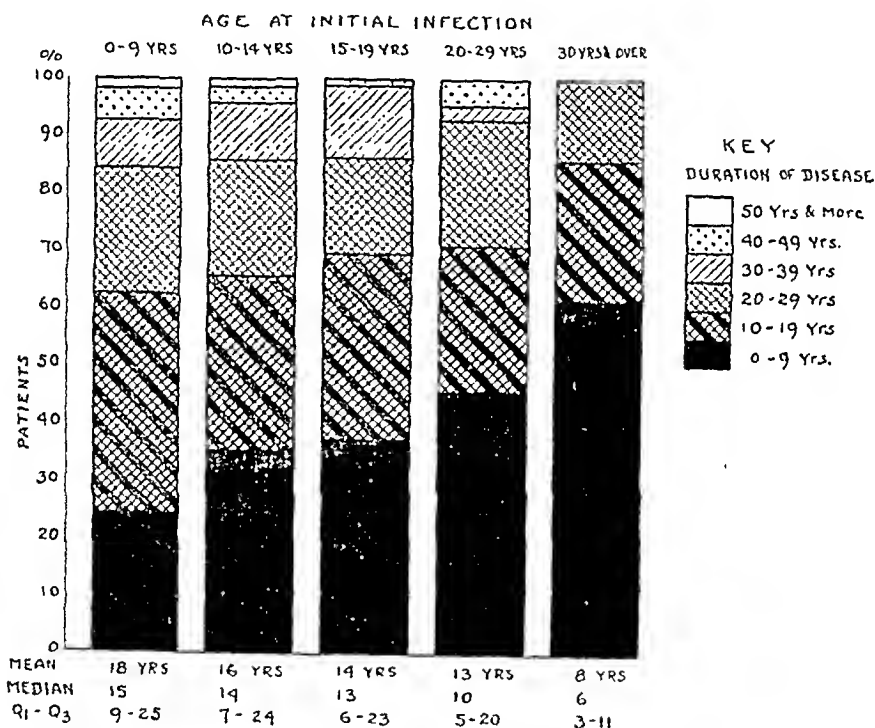


Fig. 4.—Duration of disease related to age at initial infection.

CARDIAC INSUFFICIENCY

The date at which a patient affected with rheumatic fever begins to suffer from impairment of his heart is an important landmark. Increasing fatigue and dyspnea on effort constitute the chief evidence. Other causes such as anemia and thyrotoxicosis must be excluded. The clinical phenomena are such as change a patient from Class I to IIA or IIB.[†]

Onset of Symptoms.—Symptoms of cardiac insufficiency were experienced by nearly all patients (96.2 per cent). The mean interval be-

*Space does not permit publication of these curves.

†Provided, of course, that the functional disability was due to cardiac insufficiency.

tween the onset of infection and the first clinical evidences of cardiac insufficiency was 11 years. It is noteworthy that 22.9 per cent of the patients presented symptoms within a year after the first manifestation of infection (Fig. 5). In more than one-half the patients, the interval free from symptoms was less than 10 years.

Analysis of Grant's⁶ records places the mean interval between onset of infection and the beginning of cardiac symptoms likewise at 11 years; Romberg¹⁰ found it to be 7 years in two-thirds of his cases and longer in the rest; Friedberg and Tartakower⁹ 19.6 years in their first and 33.9 years in their second group. If, as we suspect, their series are made up of the more fortunate survivors, this longer period of good cardiac reserve may be explained.

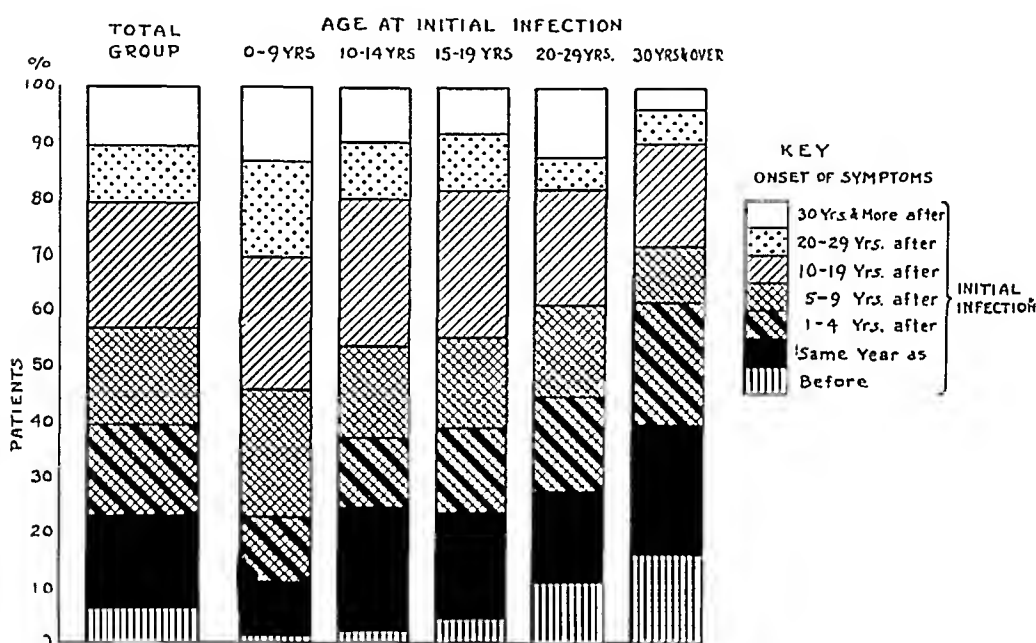


Fig. 5.—Interval between initial infection and onset of symptoms.

As might be expected from the data already presented on the duration of life, the older the patient when he is first afflicted with rheumatic infection, the shorter is the interval before cardiac symptoms make their appearance (Fig. 5).

There is a small group in which symptoms of cardiac insufficiency occurred before the onset of initial infection (Fig. 5). It is possible that in these patients the symptoms were not due to cardiac insufficiency. On the other hand, it may be, as has been stated, that the age given as that of the initial infection is incorrect and preceded the age obtained. This is especially likely among individuals said to be infected after the second decade. In every case the attempt was made to find the earliest evidence of cardiac insufficiency. It is not likely that errors were made in many instances, for the intervals between the appearance of symptoms of heart failure and death were short.

Once patients complained of symptoms of cardiac insufficiency, life expectancy was brief. The mean duration of life was five years. Fifty per cent died within from three to four years after symptoms first appeared (Fig. 6).

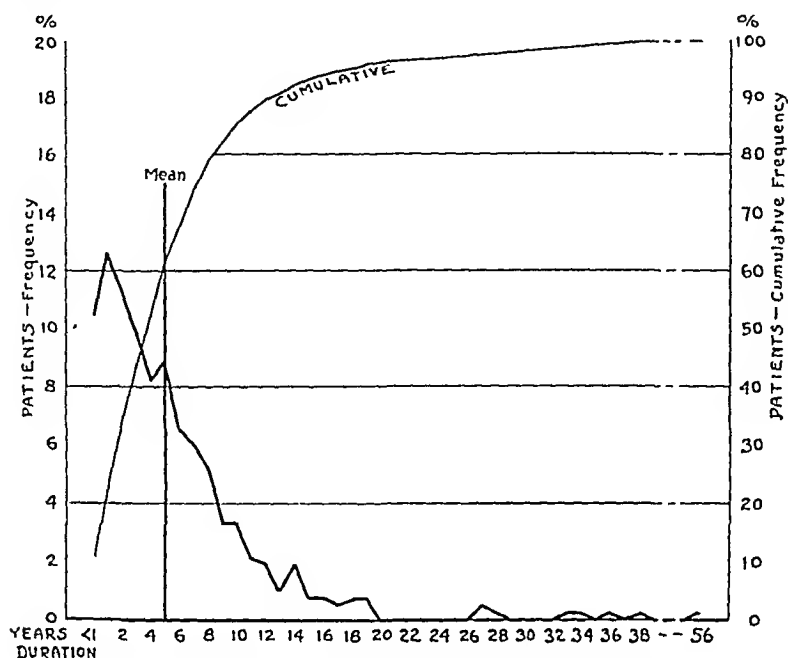


Fig. 6.—Duration of life after onset of symptoms.

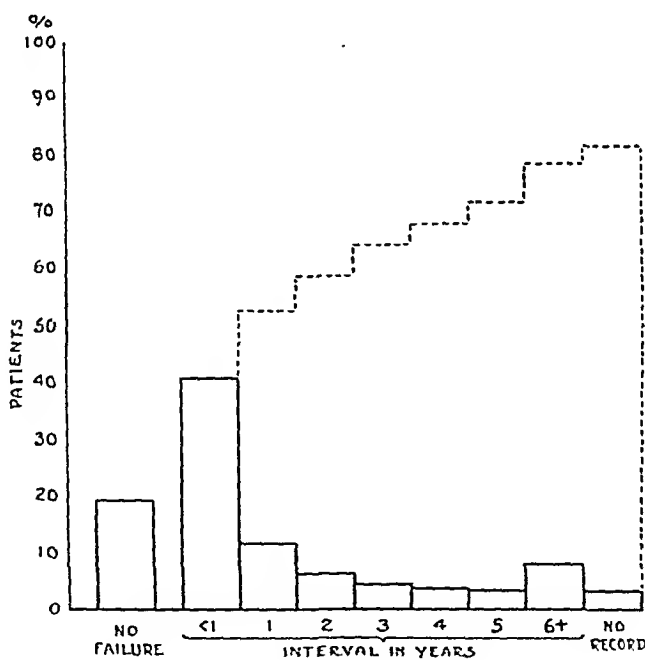


Fig. 7.—Interval between onset of symptoms and first attack of heart failure.

Heart Failure.—Heart failure has been taken to exist when the symptoms of cardiac insufficiency are so pronounced that patients are unable to do any work, but go to bed and remain there for some time. Heart failure may be due to many different causes, among them rheu-

matic infection itself. An attempt was made to ascertain the cause of failure in each case, but this was unsuccessful—probably because of the lack of proper criteria.

About 80 per cent suffered at least one attack of heart failure (Fig. 7). In general, patients began to experience attacks of heart failure about two years after symptoms of cardiac insufficiency had made their appearance. In the remaining 20 per cent either its occurrence was not recorded or the data were inadequate. Of the latter a few may have experienced heart failure before death. This group includes, however, those patients in whom the natural course of rheumatic heart disease was shortened by one of the fatal complications, such as cerebral embolism, subacute bacterial endocarditis, or an intercurrent infection.

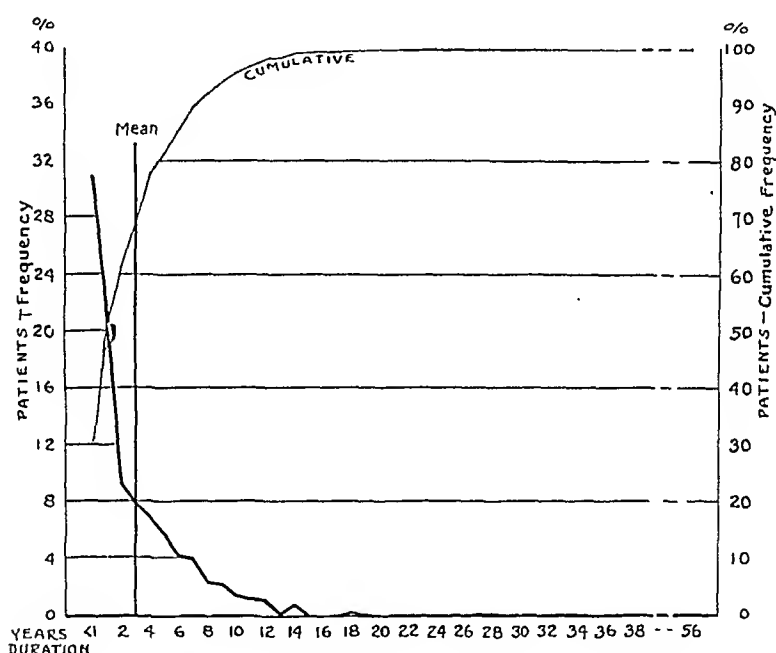


Fig. 8.—Duration of life after first attack of heart failure.

Duration of Life After First Attack of Heart Failure.—The mean duration of life after the first attack of heart failure was three years; in 75 per cent less than five years (Fig. 8). On the basis of this experience, the chances that a patient will be alive one year after the onset of heart failure are even; the chances that he will be alive five years are 1 to 4. The experience of Friedberg and Tartakower⁹ was similar to this; the mean duration was 2.5 years, and one-third of the patients lived for only one year. When Grant⁶ says that prognosis depends on “the degree of cardiac enlargement and the grade of cardiac failure, as estimated first by exercise tolerance and secondly by the presence of venous congestion,” he says in effect what is pointed out here; namely, that once a patient is in heart failure, his course is almost run.

DEATH

Age at Death.—The mean age at death was 33 years, the median about the same and the interquartile range extended from age 23 to 42 years (Fig. 9). Study of this group of 644 patients leads to the conclusion that although it is possible for patients to live for years, even beyond 70, three-fourths do not survive much beyond age 40, and about half are dead before 33 years. If patients contract the disease in adult life or survive the first two decades of life, death is most common between ages 30 and 39 (30 per cent); in the first half of this decade 15.2 per cent died, more than in any other 5-year period. Only about 10 per cent survived the fifth decade (Fig. 9). This distribution is practically the same as that found by Cabot,⁷ Willins,¹¹

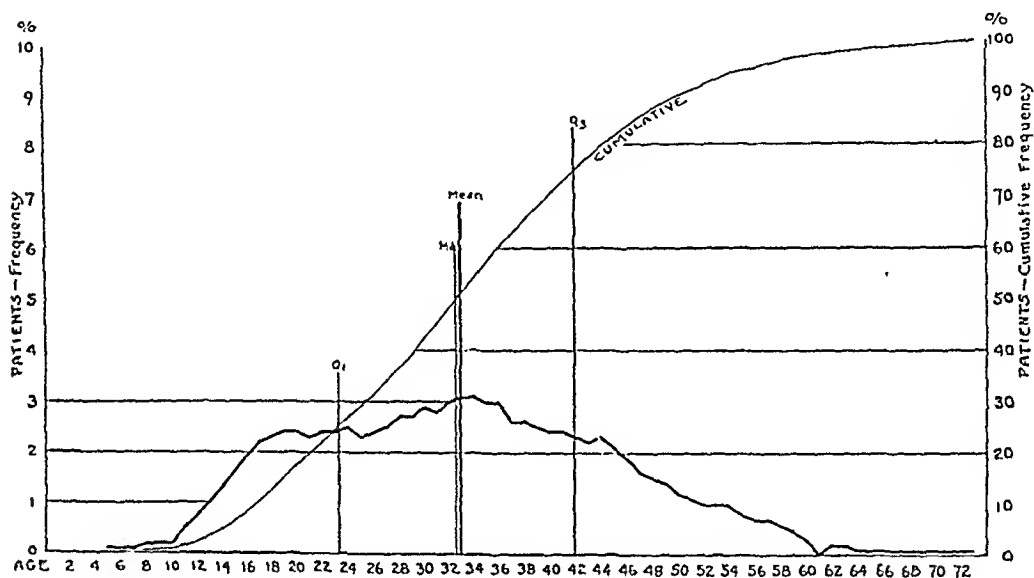


Fig. 9.—Age at death.

and Grant.⁶ A study of Grant's⁶ data places the mean age at death at 36 years; three-fourths died before age 43 was reached. Recently Davis and Weiss¹² published a similar analysis. In order to make the two groups exactly comparable those cases in the present report were tabulated separately in which death was due to heart failure; the mode again fell in the fourth decade, and less than 10 per cent of patients survived the fifth decade (Table II). When the age at death from causes other than heart failure was considered, a mode was found in the third decade, but at the same time nearly 15 per cent survived the fifth decade. The higher age at death (37 years) in Davis and Weiss's¹² cases cannot, therefore, be explained by their selection of cases to exclude causes of death other than cardiac. The difference between their figures and Cabot's and these probably has something to do with the original sampling.

TABLE II

AGE GROUPS	DAVIS AND WEISS	DE GRAFF AND LINGG		
		DEATHS DUE TO		
		HEART DISEASE %	HEART FAILURE %	CAUSES OTHER THAN HEART FAILURE %
0- 9	3	1.1	0.7	—
10-19	17	16.4	16.6	11.6
20-29	12	23.3	22.8	28.2
30-39	21	29.2	30.8	27.1
40-49	24	21.2	20.0	18.2
50-59	13	7.1	7.3	12.1
60-69	10	0.9	1.1	2.8
70-79	—	0.7	0.7	—
Mean	37	32.6	32.7	34.2
Median	38	33.0	33.0	34.0
Q ₁	24	23.0	23.0	25.0
Q ₃	50	42.5	42.5	44.5

The method of sampling may also explain the figures published by Friedberg and Tartakower⁹ who give 53 years as a mean age at death. They state that although the duration of life after first infection decreases as the age at initial infection increases, the age at death remains the same, regardless of when the onset of infection occurs. The same inference could not be drawn from a study of this series. The decade claiming the greatest number of deaths was always the decade following that in which initial infection occurred (Fig. 10).

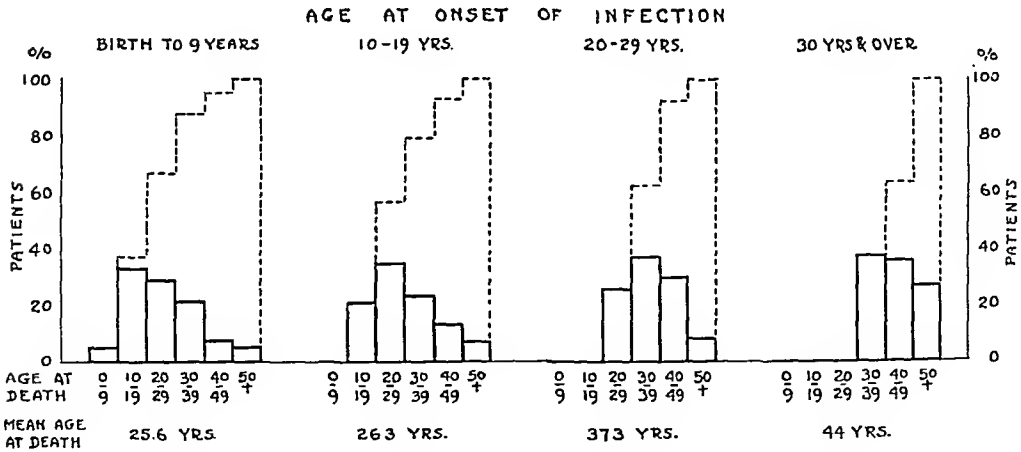


Fig. 10.—Age at death related to age at initial infection.

Causes of Death.—Causes of death were divided first into two general groups, those due to heart disease and those due to some other cause. In many cases it was possible further to subdivide the cardiac deaths. Death was usually due to heart disease (74.2 per cent), the largest group (45 per cent) dying of congestive heart failure, and 5.6 per cent dying of bacterial endocarditis. A diagnosis other than

"heart disease" was impossible in 23.6 per cent. Embolism, infarction or thrombosis and other diseases claimed, respectively, 9.2 per cent and 9.9 per cent. Among patients suffering from rheumatic heart disease the chances of dying a cardiac death are therefore 3 to 1, and the chances of dying of other diseases not referable to the circulatory system are 1 to 9.

The presence of certain conditions in the course of rheumatic infection which eventually lead to death shortens the duration of life in varying degrees. In the case of subacute bacterial endocarditis, for example, 23 of 28 patients died within 14 years, and 15 (50 per cent) within less than 8 years. In pneumonia as a cause of death a comparable situation is present. Of 13 patients, 8 died within 14 years. Of 21 patients the subject of embolism 12 died in less than 13 years. *The Medical Impairment Study* published in 1929 by the Actuarial Society of America and the Association of Life Insurance Directors¹³ indicated rather broadly that shortening of life expectancy by complications such as have been noted may be expected.

DISCUSSION

It is possible that in confining the analysis of the course of disease to the 644 patients who died, the usual course of the disease has been placed in a most unfavorable light. In order to discover whether this is the case, we analyzed briefly the records of the 609 patients who were known to be alive in 1931.

As a group, these living patients were somewhat younger (about 5 years) when they first came under observation. They were about 2 years younger when first infected. The duration of disease, so far, has been slightly less (mean 14 years, median 12 years, quartiles 9 and 21 years). Only 183 (30 per cent against 80 per cent) have, however, so far developed heart failure, but their duration of life has already been longer (mean 17 years, median 16 years, quartiles 9 and 24 years). In the remaining 70 per cent (426 patients) the life span of the disease has so far been about 2 years less than in the group that died (mean 13 years, median 10 years, quartiles 6 and 17 years). It is possible that the fact that those still living were younger at the time of initial infection accounts for their slightly greater longevity.

Unfortunately there is here no conclusive evidence that can be brought to bear on the question raised. Whether the 644 cases studied present the normal or more unfavorable course of disease, and if so, to what degree, must remain a matter of conjecture. The period, that is to say the calendar year, in which infection was acquired may be determining in its course. The effort will be made to study the subsequent histories of the patients still alive.

SUMMARY AND CONCLUSIONS

The course of rheumatic heart disease; based on the 644 patients who are dead in a total of 1,633 patients coming under observation in the 10 years up to 1931, has been described. Of these patients 55.8 per cent were males and 44.2 per cent were females. Rheumatic heart disease usually existed alone (94.5 per cent) and was seldom combined with other etiological types (5.5 per cent).

It is readily seen that this disease is in the main one of childhood and early adult life, for it occurs and runs its course chiefly within

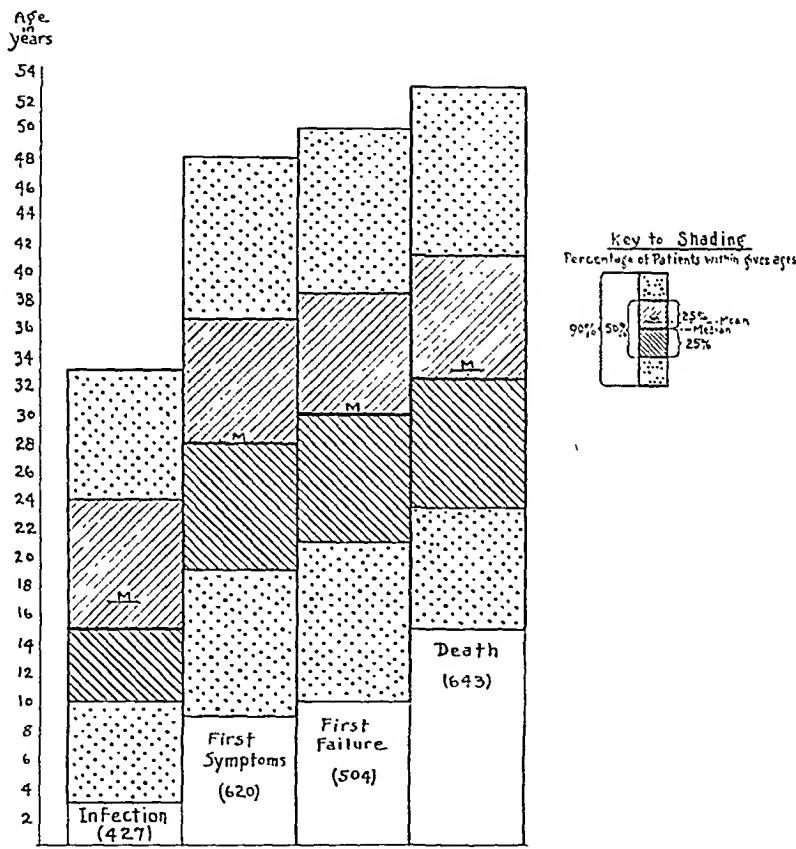


Fig. 11.—Age at occurrence of initial infection, first cardiac symptoms, first attack of heart failure, and death.

How to read chart. Example: The median age of patients at the time they were first infected is 15 years (indicated by heavy black line across first column); 50 per cent of the patients were first infected between ages 10 and 24; 25 per cent between 10 and 15 (indicated by diagonal shading); 90 per cent were infected between the ages 3 and 33 (indicated by stippled shading).

the first four decades. After age 40 there is a small proportion of sufferers. Three-fourths of those who survived to adult life are already dead. The average age at initial infection is 17 years; at the first symptoms of cardiac insufficiency 28 years; at the first appearance of heart failure 30 years, and at death 33 years (Fig. 11). Stated in another way, the average patient is infected at age 17, but will be free from symptoms and able to carry on ordinary physical activity

for 11 years. He will then begin to suffer from diminished cardiac reserve culminating in heart failure 2 years later. From this time to death, 3 years later, he is wholly an invalid or at least, in most cases, seriously incapacitated. The period of economic usefulness of a person afflicted with rheumatic heart disease is, on the average, not more than 11 years after initial rheumatic infection; in most cases less than 9 years. Once symptoms of cardiac insufficiency appear, heart failure and death follow rapidly. Fifty per cent suffer their first symptoms and failure and die within a period of from 16 to 20 years, or between 20 and 40 years of age, the years of early maturity. To see even terminal stages of this disease after the age of 50 years is not a common experience.

Death usually occurs as a result of a failing heart, but life is shortened in a fair proportion of cases by such conditions as subacute bacterial endocarditis, pneumonia, and other diseases.

The authors wish to express their indebtedness to the many doctors who have worked week after week for many years in the Adult Cardiac Clinic at Bellevue Hospital and by their work have made possible the accumulation of information that has been used in this paper.

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THE COURSE OF RHEUMATIC HEART DISEASE IN ADULTS*†‡

II. THE INFLUENCE OF THE TYPE OF VALVULAR LESION ON THE COURSE OF RHEUMATIC HEART DISEASE

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IN A previous paper the course of rheumatic heart disease from onset to death in 644 patients was described. Certain aspects of the disease were analyzed, but a discussion as to how the various valvular lesions modify its course was reserved for this paper. Reference should be made to the previous paper¹ for the source of the data and the methods of analysis employed.

The best approach to a description of the influence of the valves affected on the course of this disease may be that of a pathologist. For this reason de la Chapelle, Graef and Rottino² studied the cases which came to autopsy during thirteen years from the Third Medical Division of Bellevue Hospital. The difficulty with this method is that the number of cases with adequate clinical records becomes too small for proper analysis. Only 119 cases were found suitable. For prognostic purposes it is desirable to establish signs descriptive of an underlying lesion. Signs were established in the 644 cases now presented. Clinical records are available in 45 per cent of the patients studied post-mortem by de la Chapelle, Graef and Rottino. Although only 13 per cent of the total number came to autopsy, the study of these served to illustrate the degree of closeness with which clinical and post-mortem diagnoses corresponded.

The diagnostic criteria employed were those of the Heart Committee of the New York Tuberculosis and Health Association;³ accuracy of diagnosis was assured by insisting upon complete studies in each case. § There is probably a difference in the degree to which various valvular lesions can be accurately diagnosticated. For example, mitral stenosis can with care be recognized ultimately in nearly every instance. Concerning other valvular lesions, the criteria are, however, not so clear,

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and errors are more likely to occur. The error is probably greatest in deciding on the presence of tricuspid and pulmonic lesions (Table I).

TABLE I
CLINICAL AND POST-MORTEM DIAGNOSIS OF VALVULAR LESIONS

VALVULAR LESIONS	PERCENTAGE OF CASES IN WHICH POST-MORTEM DIAGNOSIS AGREED WITH CLINICAL DIAGNOSIS
Mitral stenosis	95
Aortic lesions	58
Tricuspid or pulmonic lesions	15

INCIDENCE OF TYPES OF VALVULAR LESIONS

The mitral valve, as has been pointed out by other observers, was found to be most frequently affected. Painsstaking anatomical studies have shown that the mitral valve is involved in almost every case of rheumatic heart disease. Coombs⁴ found evidence of this injury in every one of 97 cases, and in the cases at the Bellevue Hospital it existed in all but a few instances.² Yet, clinically, slight valvulitis may cause little or no detectable incompetence or stenosis.

Mitral stenosis, usually combined with mitral insufficiency but with no other valvular lesion, was recognized clinically in 62.5 per cent (402) of cases. This incidence is practically identical with that found post-mortem by de la Chapelle, Graef and Rottino,² but is higher than that reported by Cabot⁵ and that computed from data published by Grant⁶ and lower than that reported by Willius⁷ (Table II).

TABLE II
INCIDENCE OF VALVULAR LESIONS

LESION	DEGRAFF AND LINGG	CABOT	WILLIUS	GRANT
Mitral stenosis	62.5%	51.5%	77.0%	44.0%
Mitral and aortic lesions	28.6%	19.2%	9.3%	39.2%

Combined mitral and aortic lesions were recognized in 28.6 per cent (184) of cases. This is higher than the figure reported by Willius⁷ and by Cabot,⁵ but lower than that calculated from Grant's⁶ reports (Table II). Five of the 184 patients were infected also with syphilis. In such cases it is impossible to tell, clinically, whether aortic insufficiency is luetic or rheumatic; but the probability of its rheumatic origin, certainly in the presence of organic mitral disease, is very strong. Even if these five cases were omitted, however, the incidence would be higher than that either of Cabot⁵ or of Willius.⁷ Mitral or aortic lesions complicated by pulmonic or tricuspid lesions occurred in 29 (4.5 per cent) instances.

The incidence of other valvular lesions was small. The relative rarity of mitral insufficiency (12 cases, 1.8 per cent) alone has already been pointed out by Cabot.⁵ The very low incidence of aortic insufficiency (8 cases, 1.2 per cent), unaccompanied by other valvular lesions, is not the experience of other observers. It is possible that cases of pure aortic insufficiency were included among those of combined mitral stenosis and aortic insufficiency, especially if a Flint murmur were mistaken for the murmur of mitral stenosis. It is also possible, on the other hand, that cases of pure aortic insufficiency not of rheumatic origin may have been classified by other observers as rheumatic. That this is not improbable is borne out by experience in anatomical post-mortem diagnosis at Bellevue Hospital,² according to which uncomplicated rheumatic aortic insufficiency was found to be rare; its incidence was, in fact, similar to that found clinically. Aortic stenosis accompanied aortic insufficiency in combined mitral and aortic lesions in 39 cases. In 9 patients (1.4 per cent) valvular lesions appeared in acute terminal carditis, death occurring before a diagnosis of chronic valvular disease could be made.

Incidence of Types of Valvular Lesions by Sex.—Although more males (55.8 per cent) than females (44.2 per cent) appear to be afflicted with rheumatic valvular disease,¹ mitral valvular disease seems for some reason to be more common among females (76 per cent as against 58 per cent). Disease of the aortic valve appears, on the other hand, to be twice as common among males (40 per cent as against 22.8 per cent^{5, 7, 8}).

TYPE OF VALVULAR LESION RELATED TO AGE AT ONSET OF INFECTION

Patients who are infected early, in the first decade, are more likely to develop aortic, and even tricuspid and pulmonic, lesions (49.5 per cent against 34.9 per cent). Among individuals infected later, uncomplicated mitral stenosis is more common (60 per cent as against 45 per cent). Aside from this apparent trend no other significant relationship was noted.

TYPE OF VALVULAR LESION RELATED TO DURATION OF DISEASE

The valve involved seems to exert no influence on the duration of life with the exception of the pulmonic and tricuspid valves, which render prognosis slightly less favorable (Fig. 1). The small number of cases of pure aortic lesions forbids the drawing of conclusions. An attempt is made later, under causes of death, to explain the apparently unfavorable prognosis in cases of uncomplicated mitral insufficiency. Patients with aortic stenosis are regarded by Cabot⁵ as the longest lived in the rheumatic group, but he based this conclusion apparently on age at death and not on duration of disease. It has long been known

that aortic stenosis without other valvular lesions is relatively common in older people, but its origin, whether degenerative or inflammatory, is obscure. If inflammatory, it must be considered, it is said, as rheumatic. Only one such case was found, and this patient lived for twenty-five years after the onset of disease.

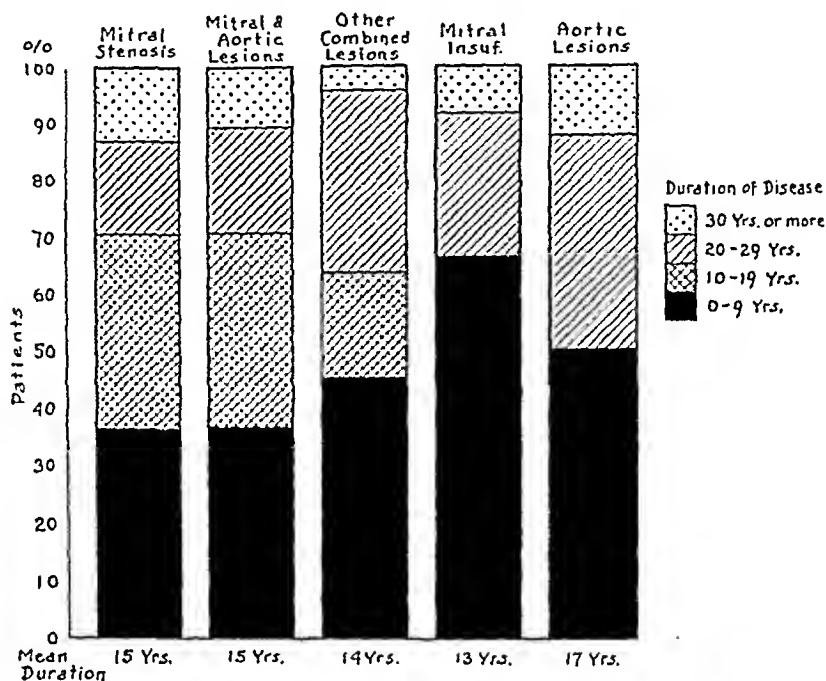


Fig. 1.—Duration of disease by valvular lesions.

Both Cabot⁵ and Willius⁷ reported a considerable difference in the duration of life depending on which valve was affected (Table III), but Friedberg and Tartakower⁸ did not regard the nature of the valvular lesion as of primary importance in prognosis.

TABLE III
TYPE OF VALVULAR LESION RELATED TO DURATION OF LIFE

	LESIONS		
	MITRAL STENOSIS	MITRAL AND AORTIC	AORTIC
Willius ⁷	12 yr.	16 yr.	22 yr.
Cabot ⁵	15 yr.	3 yr.	—
DeGraff and Lingg ³	15 yr.	15 yr.	17 yr.

TYPE OF VALVULAR LESION RELATED TO SYMPTOMS OF CARDIAC INSUFFICIENCY

The type of valvular lesion does not influence the *time* of development of symptoms of cardiac insufficiency. The average interval after the onset of the initial infection was about the same regardless of the type or number of valvular lesions (Table IV). Nor does the type of lesion appear to make much difference in duration of life after the

development of symptoms except in the case of aortic lesions. The small number of patients in this class renders inference of little value (Fig. 2).

TABLE IV
INTERVAL FROM INITIAL RHEUMATIC INFECTION TO FIRST SYMPTOMS
OF CARDIAC INSUFFICIENCY

VALVULAR LESIONS	MEAN	MEDIAN	Q ₁ - Q ₃
Mitral stenosis	10 yr.	7 yr.	Less than 1 yr. to 15 yr.
Mitral and aortic	9 yr.	5 yr.	Less than 1 yr. to 15 yr.
Aortic	9 yr.	6 yr.	Less than 1 yr. to 11 yr.

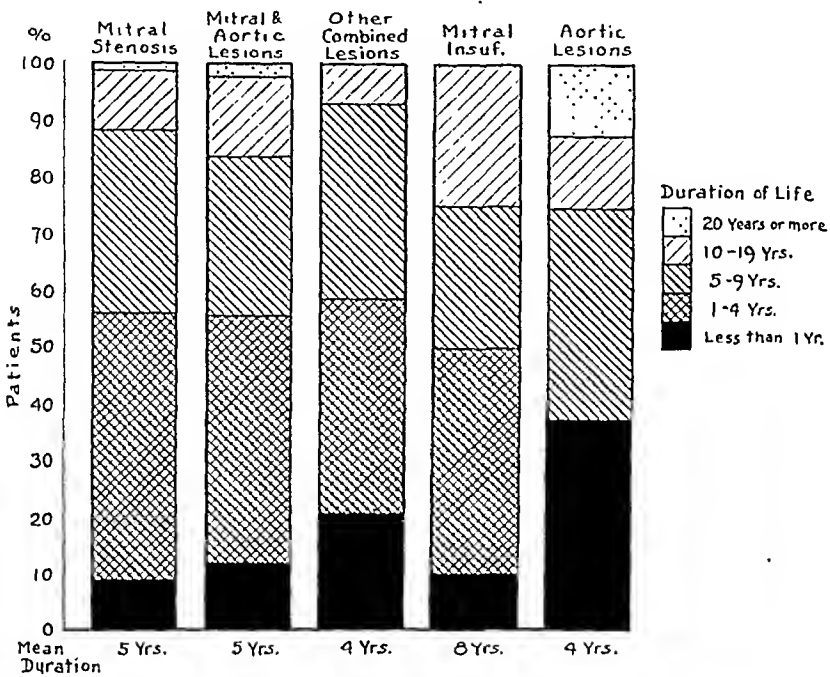


Fig. 2.—Duration of life after onset of symptoms by valvular lesions.

TYPE OF VALVULAR LESION RELATED TO CONGESTIVE HEART FAILURE

Heart failure with congestion appeared at about the same time (mean age 31 or 30) whether mitral stenosis or mitral and aortic disease was present. In the aortic group, it appeared earlier if it appeared at all, but more than one-third escaped congestive heart failure altogether, as far as is known, and the remainder is too small to warrant analysis. The average duration of life after the appearance of heart failure in mitral stenosis and in mitral plus aortic disease was brief (Fig. 3). In aortic lesions it was longer (7 years), but here again, because of the small number of cases, conclusions drawn now would be misleading.

The mean duration of life in patients with mitral insufficiency, after the appearance of congestive heart failure, was less than one year, but there were only 12 cases altogether.

CAUSE OF DEATH RELATED TO TYPE OF VALVULAR LESION

Death was usually due to some form of cardiac disease. In mitral stenosis, 70 per cent, in mitral and aortic valvular disease, 79 per cent, in disease of the tricuspid or pulmonic valve, 90 per cent, and in aortic valvular disease 75 per cent of the patients died cardiac deaths.

Congestive heart failure was the type of cardiac death most frequently seen, especially when the pulmonic or tricuspid valve was involved (in 83 per cent), but a little less often when only one valve was diseased, as, for example, in aortic insufficiency (25 per cent) and in mitral insufficiency (25 per cent). In the former, however, 75 per cent died cardiac deaths; in the latter only 41.6 per cent, while one-

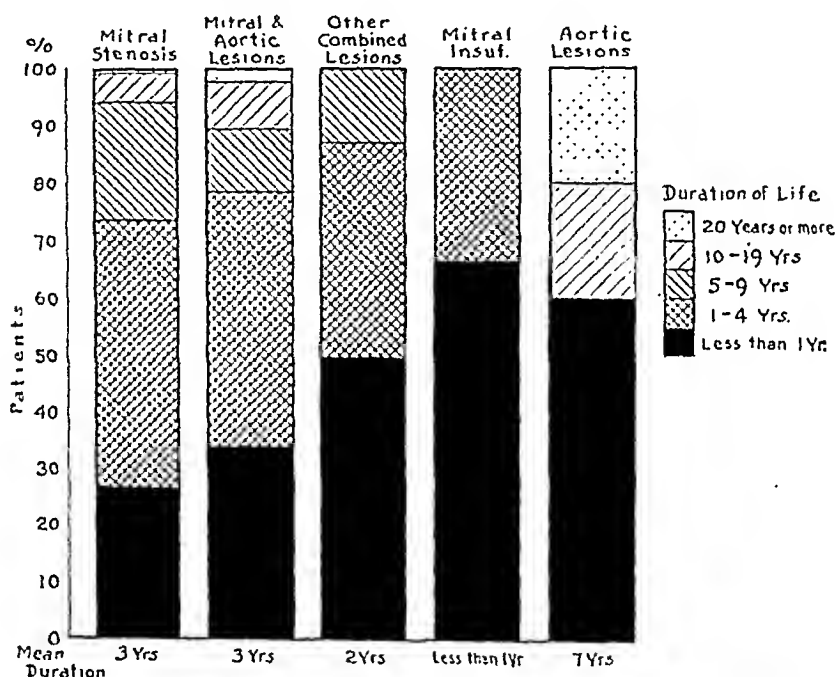


Fig. 3.—Duration of life after onset of heart failure by valvular lesions.

third died of other diseases, a much larger proportion than in any of the other groups. This may explain the apparently unfavorable prognosis already referred to.

It appears then that whereas among patients suffering from rheumatic heart disease the chances of dying cardiac deaths are in general 3 to 1, in mitral insufficiency they are only 1 to 1.4, and the chances of dying of other diseases not related to the circulatory system are 1 to 2. Slightly fewer patients with mitral stenosis died in congestive failure than patients suffering aortic disease combined with mitral stenosis (42 per cent against 48 per cent). The chances of developing congestive failure are greater, it seems, the greater the number of valvular lesions.

In agreement with other observers,¹⁰⁻¹⁵ we found that subacute bacterial endocarditis was an infrequent cause of death in uncomplicated mitral stenosis (9 cases). It occurred more often when the aortic valve was diseased (16 cases).

SUMMARY AND CONCLUSIONS

An analysis of the effect of the type of valvular lesion on the course of rheumatic heart disease has been presented, based on the records of 644 patients who died. The importance of using for analysis data obtained during the life of the patient rather than the records from autopsies has been discussed. The incidence of the various valvular lesions is given. Mitral valvular disease was found to be more frequent in women, whereas aortic disease was approximately twice as frequent in men. The age at initial infection seemed to influence the type of subsequent valvular lesion only so far as the first decade of life is concerned. In a larger proportion of patients infected before age 10 than among those infected later in life, more than one valve was affected. The valve affected did not seem to influence the duration of life except in the case of the pulmonic or tricuspid valves. In the presence of damage to these, prognosis became slightly less favorable than when mitral stenosis appeared either alone or in combination with aortic lesions. In considering the relatively short duration of life observed in cases of mitral insufficiency alone, the high incidence of deaths due to other than cardiac or circulatory diseases must be taken into account.

The interval from initial rheumatic infection to the appearance of symptoms of cardiac insufficiency or congestive heart failure and the subsequent duration of life were about the same regardless of the valve or the number of valves affected.

Most of the patients died cardiac deaths, the incidence apparently being higher the greater the number of valvular lesions. Congestive heart failure appeared more frequently as a cause of death when disease of more than one valve was present; and subacute bacterial endocarditis when the aortic, tricuspid or pulmonic valve was diseased.

The evidence here presented lends support to the statements made by Flint¹⁶ in 1862, by Mackenzie¹⁷ in 1925, and more recently by Grant,⁶ that valvular disease in itself gives no information as to prognosis.

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RHEUMATIC HEART DISEASE

IV. THE LIFE HISTORY OF THE SEVERE FORM OF THE DISEASE*

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CLINICAL DURATION OF RHEUMATIC INFECTION

KNOWLEDGE of the time of onset of rheumatic infection and the age at death is essential in a study of the life history of rheumatic heart disease. In previous communications the age distribution at death in a group of patients with rheumatic heart disease was presented.^{1, 2} Corresponding statistical data showing the onset of the rheumatic infection leading to heart disease are difficult to obtain because of the well-recognized fact that advanced cardiac damage not infrequently occurs without any recognized clinical manifestation of the rheumatic infection, and because at times cardiac lesions precede the first recorded attack of rheumatic fever. Some idea of the duration of the disease can, nevertheless, be obtained by assuming that the first recorded attack of rheumatic fever represents the time of onset of the infection. The error in such an assumption would make the average duration of the disease longer than that indicated by the clinical data to be presented. This error is counteracted, on the other hand, by the fact that in some instances the onset of cardiac damage may have been independent of the first attack of rheumatic fever.

The duration of rheumatic heart disease was studied in a group of patients with necropsies, in whom rheumatic heart disease was eventually the cause of death. An earlier analysis showed that of 369 patients with unquestionable rheumatic heart disease, 44 per cent died of this disease; in 11 per cent rheumatic heart disease was a contributing cause; in 17 per cent death was due essentially to subacute or acute bacterial endocarditis on a rheumatic basis; and in 27 per cent it was due to causes not associated with rheumatic heart disease. The data presented in this communication bear only on cases in which death was caused by rheumatic heart disease.

Age of Onset. The clinical data in 108 cases with necropsies clearly indicated whether or not there had been a previous rheumatic infection. Eighty-three of these cases, 40 males and 43 females, gave a definite history and 9 a suggestive history of either rheumatic fever

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or chorea. In 16 cases there was no recollection of any previous rheumatic manifestation. Thirty additional cases were included with a definite history of rheumatic infection but without necropsy studies, making a total of 113 cases with positive rheumatic histories.

TABLE I
AGE OF ONSET OF FIRST ATTACK OF RHEUMATIC FEVER IN 113 CASES

AGE GROUP	CASES	
	No.	Per Cent
Years		
0-10	31	27.4
11-20	46	40.8
21-30	16	14.1
31-40	14	12.4
41-50	4	3.5
51-60	1	0.9
61-70	1	0.9
71-80	0	0.0

Table I shows the distribution according to age of onset of rheumatic fever or chorea. The earliest age of onset was three years; in 3 cases infection was acquired at five years. The majority of instances in the first decade, however, occurred nearer the age of ten years. In accordance with general knowledge, a high percentage was noted in the first and second decades, 77 patients having had their first attack before the twentieth year. A smaller but appreciable group apparently acquired the infection in the third and fourth decades, and 4 in the fifth decade. In one instance the first and fatal attack occurred in the sixty-first year, and gross and histological evidence of a typical acute rheumatic pancarditis was found on post-mortem examination.

Relation of First Attack to Onset of Cardiac Damage. Some opportunity to answer the question as to whether the first recorded attack of rheumatic fever was coincident with the earliest cardiac damage was presented in 10 cases in which a first attack of rheumatic fever resulted in a fatal attack of heart disease. In 5 of these 10 cases, valvular and myocardial lesions were entirely acute; there was no gross or microscopic evidence of a past infection as indicated by chronic inflammatory reactions. In the group showing evidence of old rheumatic heart disease the degree of involvement was slight in 3 patients and marked in 2. The ages of the 5 patients with acute lesions were 13, 22, 35, 35, and 61 years; the ages of those showing fresh as well as old lesions were 11, 15, 19, 22, and 35 years. The duration of illness in 8 of these 10 patients was one month or less; in 2, six and eight months.

In this group of 10 cases, then, the onset of the first recorded rheumatic infection corresponded with the onset of demonstrable rheumatic heart disease in but 50 per cent. Deductions as to the significance of the first recorded attack cannot be drawn from so small a group. It

is interesting, however, that onset of rheumatic carditis should so often—in 4 out of 5 cases—be associated with an attack of rheumatic fever occurring for the first time in adult life.

Duration of Life After First Attack. The duration of life after the first recorded attack of rheumatic fever in 83 fatal cases is shown in Table II. Twenty-five patients lived five years or less, 6 having died from the initial attack and 8 in less than two years from the time of onset. The remainder showed a duration of life ranging from six to

TABLE II

DURATION OF LIFE AFTER FIRST ATTACK IN 83 CASES WITH NECROPSY RECORDS

DURATION OF LIFE	CASES
<i>Years</i>	<i>No.</i>
0- 5	25
6-10	10
11-15	10
16-20	13
21-25	10
26-30	5
31-35	7
36-40	3

forty years after the earliest manifestation. As would be expected, rheumatic cardiac activity at death is more frequent in patients dying a short time after the first attack of rheumatic infection. In an unselected group of 21 patients in whom death occurred within three years after onset of infection, activity was noted in 18; in a second unselected group comprising 19 patients who had lived twenty-five or more years after the first infection, activity was noted in 9.

TABLE III

DURATION OF LIFE IN 36 CASES OF RHEUMATIC FEVER ACCORDING TO AGE AT ONSET OF FIRST ATTACK

18 CASES WITH ONSET BEFORE AGE OF 10	18 CASES WITH ONSET AFTER AGE OF 26
<i>Years</i>	<i>Years</i>
2	0
2	0
2	0
3	0
10	1
12	4
14	5
15	7
15	8
18	8
20	10
20	10
21	12
27	20
32	20
32	20
34	25
35	25

There is a general belief that rheumatic infection is more damaging to the myocardium in the early years of life than when it occurs for the first time after the age of twenty-five years. Table III gives the duration of life in two groups: one, in which the first attack occurred at or before the age of ten; the other, in which the first attack occurred at or after the age of twenty-six years. In the latter group the duration of life was appreciably shorter, and death followed soon after the first attack of rheumatic fever in 5 cases, whereas in the first group no immediate fatality occurred. The duration of life was approximately 30 per cent longer in Group 1. This finding suggests that the rheumatic infection is more damaging to the heart when the first attack occurs in an adult. Another possible explanation of the difference, however, may be that after adult years the first recorded attack of the rheumatic infection is less likely to represent the true onset.

DURATION OF HEART FAILURE

An analysis was made of the duration of the cardiac symptoms, as indicated by the duration of the "present illness" in 134 patients eventually dying as a result of rheumatic heart disease. The "present illness," as employed in this study, covers the period from the onset of *significant and progressive symptoms* to the time of death. In some instances in which the patients gave a history of having had symptoms for many years, the exact time of onset was not clear, either because of the insidious character of the progression, or because, as often happens, patients who are informed in early youth that they have heart disease go through life with a mild neurosis or fear of over-exertion, and date the onset of symptoms from the time of the medical diagnosis. In other and rather frequent instances there is a true but slight limitation of the cardiac reserve which remains stationary for many years, after which a definite downhill progression of symptoms occurs. Eleven of the 134 cases studied for the duration of symptoms showed an initial period of several years in which there was either such mild limitation of circulatory efficiency or a neurosis manifesting itself as such. The preliminary period in these 11 cases was not regarded as a part of the present illness.

The character of onset and the course of cardiac manifestations showed wide variation. The following are characteristic clinical groups:

1. *Acute Heart Failure and Rapid Death.* The illness is of sudden onset with severe pulmonary symptoms in a patient previously in good health. The patient is forced to bed with marked dyspnea, orthopnea, cyanosis, pulmonary congestion and edema, and dies within from two days to six weeks.

2. *Acute or Subacute Heart Failure With Recovery.* There is a relatively sudden onset of weeks or months in duration, as in Group 1, but

recovery occurs. The recovery is either complete within a few weeks, with freedom from all symptoms, or partial, with persisting dyspnea on exertion and limitation of cardiac reserve. Prognosis is difficult, for death may occur at any time within from three months to ten years, and after one or more attacks of failure. It may occur as a climax to increasing limitation of reserve, or precipitately as acute failure.

3. *Progressive Heart Failure.* In this group the onset is gradual, with slowly progressive failure over a period of from one to three years. Recovery is slight or insignificant in spite of prolonged bed rest. The cardiac reserve steadily diminishes and death ensues.

4. *Gradual Onset of Heart Failure With Recovery of Short Duration.* The onset is as in Group 3 but with some recovery after prolonged rest and digitalis. There is relative comfort for a period of several months, but rarely longer; failure then occurs and death ensues.

TABLE IV
DURATION OF HEART FAILURE IN 134 FATAL CASES

DURATION OF FAILURE	CASES	
<i>Months</i>	<i>No.</i>	<i>Per Cent</i>
1 or less	36	27
6 or less	62	46
12 or less	78	58
<i>Years</i>		
1 or more	56	42
3 or more	44	33
5 or more	19	14
10 or more	5	4
15 or more	3	2

Table IV presents the distribution of the 134 cases according to the duration of "present illness." Twenty-two patients died within two weeks from the time of onset of definite cardiac symptoms; 36 within one month; 62 within six months; and 78, or more than 50 per cent, within one year. Forty-four cases showed a duration of illness of three or more years, 19 cases of five or more years, and 5 cases of ten or more years.

TABLE V
DURATION OF LIFE AFTER ONSET OF CONGESTIVE FAILURE IN 56 CASES WITH TOTAL ILLNESS EXCEEDING 1.5 YEARS

DURATION OF LIFE	CASES
<i>Months</i>	<i>No.</i>
1 or less	11
2-6	14
7-12	4
<i>Years</i>	
1.5-3	16
3.5-5	6
6-10	5

Duration of Congestive Failure. It is of prognostic importance to obtain information as to the expectancy of life after the onset of definite congestive failure necessitating rest in bed. Accordingly, the duration of life in this stage of failure was analyzed in a group of 56 cases with a total duration of illness, including the period preceding the congestive failure, of one and one-half years or longer (Table V). In some of these cases there were one or more intervals of relative improvement after the onset of severe failure. In 27 cases, or approximately one-half, congestive failure persisted for more than one and one-half years. In 11 cases, death occurred after failure had been present one month or less.

Factors Determining an Acute Fulminating Course. One of the striking findings among these patients with rheumatic heart disease was the high frequency of acute cardiac deaths. Some of the factors which may be responsible for such a fulminating course are: active rheumatic infection, infections other than rheumatic, embolism, and pulmonary complications, including sudden general or left-sided failure with pulmonary edema. Sex apparently is not a significant factor, since in a group with an illness lasting six months or less there were 33 males and 31 females, and in a group with an illness of two years or more, 23 males and 32 females. Age, likewise, does not appear to be a related factor. A correlation of the clinical course with the post-mortem findings, on the other hand, suggests that the presence of activity, and particularly the site and degree of the activity, is of importance. Thus, in a group of 36 patients with an illness of one month or less, activity was present in 26. In a group of 29 patients with an illness of four years or longer, there was activity in 5, questionable activity in 5, and absence of active infection in 19. A comparison of these groups suggests that active carditis, if sufficiently severe, may precipitate a rapid downhill course.

In some patients *embolism* obviously resulted in a rapid course. Embolism usually occurs in the presence of auricular fibrillation, early

TABLE VI

CAUSE OF DEATH IN 36 CASES WITH A CARDIAC ILLNESS OF ONE MONTH OR LESS IN DURATION

CAUSE OF DEATH	NO. OF CASES
Embolism	8
Failure with active carditis	8
Failure without active carditis	5
Failure with active carditis and terminal infection	4
Failure with active carditis and pulmonary atelectasis	3
Failure without active carditis and with terminal infection	2
Failure with active carditis and acute nephritis	2
Failure with pregnancy	1
Failure with embolism and infection	1
Purulent pericarditis	1
Unknown	1

or late in the course of congestive failure.³ Thus in the group of 36 patients with an illness of one month or less, significant embolism occurred eight times, as compared with seven times in a group of the same size with an illness of four years or longer.

Table VI shows the clinical state just before death in 36 patients with a fulminating course. Embolism was responsible for death in 8 patients. General failure was present in 26, and in 17 of this number active carditis was found. In 7 of the 17 with active carditis, terminal infection, usually bronchopneumonia, occurred. In 3 patients with general failure and carditis, significant pulmonary atelectasis was found at the post-mortem examination. In 5 patients the final failure was unaccompanied by infection. In 1 patient general failure was apparently precipitated by the terminal months of pregnancy. In 2 patients general failure with active carditis and acute nephritis coexisted. The exact rôle of the acute nephritis in the causation of death was difficult to evaluate.

An analysis of the *degree of valvular damage* in the same 36 patients showed moderate valvulitis with stenosis of either mitral or aortic valves in 14 patients and marked changes in 2. The remaining patients showed only minor lesions of the valves, stenosis being only slight or absent in most instances. The death of patients not dying of such complications as embolism was, therefore, in all probability due to myocardial damage. The condition of the myocardium in 17 patients may have been significantly aggravated by the active rheumatic infection. In the 2 patients with marked valvular lesions there was no evidence of active infection, and it is probable that death was due chiefly to mechanical failure.

DISCUSSION

This study, as well as the data presented in previous communications,^{1, 2} confirms the common clinical observation that the course of rheumatic heart disease shows great variation. In the entire group of 474 cases there were 269 in which death was due to causes other than rheumatic heart disease.¹ In these cases, as well as in those in which cardiac damage was only partially responsible for death, it was not feasible to study the life history of the disease. The clinical course of rheumatic heart disease, as observed in the cases here analyzed, is that characteristic of cases in which cardiac damage eventually leads to death; hence the data presented are not comparable with those obtained from the study of patients irrespective of the degree of cardiac involvement.^{4, 5}

The distribution of cases in the present group according to the age at onset of rheumatic infection corresponded closely with that in the group observed clinically by Willins.⁶ Analysis according to duration of life after onset of rheumatic fever showed an approximately equal

distribution in the group less than two years, the group two to five years, and in the five-year periods up to twenty-five years. A smaller number of patients lived as long as forty years after the first infection, ultimately succumbing to the heart disease. Since duration of life varies so greatly, one cannot speak with justification of the average duration of life after the first infection. Prognostication as to expectancy of life after the first infection is, therefore, not feasible. In accordance with the findings of Willis,⁶ there is some tendency toward a shorter duration of life when the first infection develops after the age of twenty-five years than when this occurs before the age of ten years. This difference cannot be explained by the shorter expectancy of life after the age of twenty-five years. A probable interpretation is that adults are less tolerant to rheumatic cardiac infections.

The fact that in many cases the duration of life is short following the appearance of cardiac symptoms, and particularly following the onset of congestive failure, is significant. Thus, of the patients presenting these symptoms, 58 per cent were dead within a year after the onset of cardiac symptoms. As high as 27 per cent exhibited cardiac symptoms or signs of less than one month's duration. Age and sex, as well as the distribution and the degree of valvular damage, played no significant rôle in the precipitation of this rather acute type of cardiac death. Acute rheumatic myocarditis, embolism, and acute infections other than rheumatic fever were the most frequent precipitating factors. Laws and Levine⁷ have also emphasized the frequency of death resulting from causes other than chronic failure of the myocardium.

SUMMARY

1. Data are presented bearing on the course of fatal rheumatic heart disease as obtained from the records on 113 cases and 83 necropsy examinations.

2. The age at onset of the first rheumatic infection varied from three to sixty-one years, the majority of cases occurring in the first and second decades.

3. The duration of life after the onset of clinical evidence of rheumatic infection varied from a few weeks to forty years. About 50 per cent of the patients lived from six to twenty-five years, the number of cases showing fairly even distribution according to five-year intervals.

4. More than 50 per cent of the patients died within one year after the onset of definite cardiac failure.

5. The clinical types of heart failure encountered are described, and the high frequency of relatively short duration of life following the onset of significant cardiac symptoms, and particularly of congestive

failure, is analyzed. Almost one-third of the patients succumbed as a result of a fulminating course precipitated by factors other than chronic myocardial failure.

6. In the fulminating fatal course acute carditis, embolism, and infections other than rheumatic fever played the most significant rôles.

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THE TWO-STEP TEST OF MYOCARDIAL FUNCTION*

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FOR many years, tests of myocardial function have been a common procedure in physiological and medical institutions and also in the office of the medical practitioner. The large number of reports and the variety of methods described, however, suggest that a satisfactory routine test has not been found. The tests in the main are not for quantitative measurement, and the few that are measurable have no standards for normal individuals in relation to sex, age, and weight. Another important criticism is that many methods utilize unusual muscular movements.

As early as 1889, and between then and 1904, observations¹⁻⁴ were reported showing that systolic blood pressure and heart rate rose during and directly after muscular work and declined later. In the following review of the tests described in the literature and in my own test, blood pressure and pulse rate readings made after a certain interval of time subsequent to a definite exertion are compared with the resting blood pressure and pulse rate figures before the exertion. If these two readings are practically the same, the individual is considered to have a good, or normal, myocardial function.

The form of functional test of the heart is usually some body movement, such as flexing and extending the arm, flexing the trunk, or knee-bending.⁵⁻⁹ Kahn¹⁰ introduced hopping on each foot 100 times, and all kinds of modifications of this test are in common use. For instance, the patient may be asked to hop twenty, forty or more times on each foot.

Stair climbing was in vogue for many years and is somewhat used at the present time. Selig,¹¹ as early as 1905, was an exponent of this form of test. Rapport¹² directed his patients to mount 45 and 90 steps, each 9 inches high. These climbs were made at different speeds. Wilson¹³ employed 25 and 60 steps. Although this worker made quantitative measurements, sex, age, weight and height were not taken into consideration. Magnus-Alsleben⁸ and Felberbaum and Finesilver¹⁴ also used stairs or steps—the latter built two steps each 6 inches high.

In 1901, Brittingham and White¹⁵ used dumb-bell swinging, from floor to an arm's length overhead. Barringer,¹⁶⁻¹⁹ in a series of articles published between 1915 and 1922, popularized this type of test, and

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Mann²⁰ applied it to the study of patients during convalescence. Cotton, Rapport and Lewis²¹ considered the total work done. Barringer¹⁸ demonstrated that work performed with the arm and back muscles gave the same results as work with the thighs and legs. Wilson¹³ reported that the results of stair climbing and rope jumping were similar to those of dumb-bell exercise. Barringer¹⁷ stated that the outcome varied but slightly from day to day in the same individual. It will be shown that this was found to be true, also, when the test described in this paper was used. This uniformity enhances the value of a test. In 1922, Barringer¹⁹ suggested that normal standards of exercise tolerance for adults should be worked out.

For essentially quantitative tests, one must refer to the stationary bicycle, visible but now seldom used in the physiology department of a medical school. Ergostats and ergometers, where the muscles of the fingers, arm or leg come into play, have been described by Mendelsohn,²² Gräupner,²³ Benedict and Carpenter,²⁴ Krogh,²⁵ Cathcart, Wishart and McCall,²⁶ and Gillespie, Gibson and Murray.²⁷

A criticism of the prevailing tests, as already stated, is that they either do not measure work performed quantitatively, or that the same exertion is required of male or female, young or old, light or heavy individual. Of equal moment is the criticism that no standards for normal individuals have been constructed.

In 1929, E. T. Oppenheimer and I²⁸ published an account of a "two-step" test which supplied a quantitative measurement of work. In performing this test, only ordinary everyday muscular activity is called into play, the procedure is a definite and simple one, and it may be carried out in a physician's office or in a clinic.

The subject of functional tests is reviewed for two reasons. (1) New tables* (Tables I and II) have been constructed which immediately give the required number of ascents for a given weight and age without further arithmetical calculation, and all interpolations and corrections for age and height have been obviated. (2) The later tables are based on the results of approximately 1,500 tests carried out upon

*Dr. P. V. Wells, the biophysicist of the Prudential Life Insurance Co. of America, calculated the mathematical graduations necessary for the construction of these tables.

The experimental material upon which the revised tables are based resulted from the testing of 210 males and 234 females, four to seventy-four years of age. The maximum number of ascents performed without delaying the return of the blood pressure and pulse rate to normal was recorded. From this data and the patient's weight the work performed in foot pounds per minute was calculated. The work done is recorded in terms of climbs, this being considered a better estimate of physical fitness than foot pounds, as it measures the relative efficiency of subjects in handling their weight, as it affects the circulation.

The original tables were based on partial correlation equations in terms of sex, age, and weight, but the inconsistencies in the coefficients indicated that the correlation with height was a spurious effect of the relation between height and weight.

Statistically, the process of "smoothed medians" was used. In the graduation each median was "weighted" by the actual number of cases in its age and weight class. The table of median ascents showed clearly that children of median weight accomplished over 30 ascents, while adult males of median weight did not exceed 25, and adult females reached only 23 ascents. For a given age, the numbers decreased steadily with increasing weight.

TABLE I
STANDARD NUMBER OF ASCENTS FOR MALES

WEIGHT (LB.)	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69
40-49	35	36											
50-59	33	35	32										
60-69	31	33	31										
70-79	28	32	30										
80-89	26	30	29	29	29	28	27	27	26	25	25	24	23
90-99	24	29	28	28	28	27	26	26	25	24	23	22	21
100-109	22	27	27	27	27	26	25	25	24	23	22	21	20
110-119	20	26	26	26	26	25	24	23	22	21	20	20	20
120-129	18	24	25	25	25	24	23	23	22	21	20	20	19
130-139	16	23	24	25	26	25	24	23	22	21	20	20	18
140-149		21	23	24	25	24	24	23	22	21	20	19	18
150-159		20	22	24	25	24	23	22	21	20	20	18	18
160-169		18	21	23	24	23	22	22	21	20	19	18	17
170-179			20	22	23	23	22	21	20	19	18	17	16
180-189			19	21	23	22	21	20	19	18	17	16	15
190-199			18	20	22	21	21	20	19	18	17	16	15
200-209				19	21	21	20	19	18	17	16	16	15
210-219				18	21	20	19	18	17	17	16	15	14
220-229				17	20	20	19	18	17	16	15	14	13

TABLE II
STANDARD NUMBER OF ASCENTS FOR FEMALES

WEIGHT (LB.)	AGE IN YEARS												
	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69
40-49	35	35	33										
50-59	33	33	32										
60-69	31	32	30										
70-79	28	30	29										
80-89	26	28	28										
90-99	24	27	26	28	28	27	26	24	23	22	21	21	20
100-109	22	25	25	27	27	26	25	24	23	22	21	20	19
110-119	20	23	23	25	25	24	23	22	21	20	19	18	18
120-129	18	22	22	24	24	23	22	21	20	19	18	17	17
130-139	16	20	20	23	23	22	21	20	19	18	17	16	16
140-149		18	19	22	22	21	20	19	18	17	16	15	15
150-159		17	17	21	20	20	19	19	18	17	16	15	14
160-169		15	16	20	19	19	18	18	17	16	15	14	13
170-179		13	14	19	18	18	17	17	16	15	14	13	13
180-189			13	18	17	17	16	16	15	14	13	12	12
190-199			12	17	16	16	15	15	14	13	12	11	11
200-209				16	15	15	14	14	13	12	11	10	10
210-219				15	14	14	13	13	12	11	10	9	9
220-229				14	13	13	12	12	11	10	9	8	8

444 normal persons, male and female, whereas the previously published tables were derived from a much smaller group of about 500 tests of 115 normal individuals. The tests were practically all performed at the Cornell Clinic of the Cornell University Medical College between the years 1927 and 1933.

METHOD OF PERFORMING THE TEST

The contrivance employed in this method of testing the functional condition of the heart consists of two steps,* each 9 inches high, so that one climb is one and one-half feet above the ground. (Fig. 1.) The number of ascents which the individual



Fig. 1.—Two steps, each accurately 9 inches high, are placed near a wall or table. One climb is an ascent and descent. The patient always turns toward the wall before re-commencing another ascent.

should, theoretically, perform is obtained from the tables, and is determined by the patient's age and weight. The resting blood pressure and pulse rate are taken in the sitting or lying posture and are usually obtained within three to five minutes. Readings of the blood pressure and pulse rate are repeated until two in succession are practically the same. The patient then walks up one side of the steps and down the other, always turning toward the same side of the room or table before each ascent. This necessitates a change of direction at each turn and thus giddiness with its resulting artificial changes in the blood pressure and pulse rate is prevented.

*These steps can easily be built at home or office. Dr. L. F. MacKenzie has designed a compact folding pair of steps which Beeton, Dickinson & Co., of Rutherford, N. J., have placed on the market.

In a minute and a half the patient makes his required number of ascents and then sits down. Two minutes after cessation of exercise the blood pressure and pulse rate should have returned to resting figures. Ten points difference in the blood pressure or pulse rate is the extreme limit permitted.

A definite example will be given. The work capacity of a man forty-four years of age, weighing 150 pounds, was required. In the tables, the vertical column of figures under forty-four years of age and the horizontal row opposite 150 pounds intersect at 22. This is the number of climbs or amount of work, so measured, that a normal man of this patient's age and weight should be able to perform. The blood pressure and pulse rate readings were these:

BLOOD PRESSURE	PULSE RATE
118/80	66
112/78	60
110/76	60

Obviously, the last readings were the patient's resting figures. He was started on his 22 climbs, and his rate was regulated so that he should perform exactly this number in one and one-half minutes. He then sat down again. At the end of two minutes, the readings were: blood pressure 116/78 and pulse rate 62 beats per minute, which are within the ten point difference allowed. In other words, the patient's exercise capacity was normal. The work performed was: 22 climbs \times 150 lb. weight \times $1\frac{1}{2}$ feet height = 4,850 ft. lb. This work, however, was done in $1\frac{1}{2}$ minutes. Per unit of time, that is, per minute the work was: $\frac{22 \times 150 \times 1\frac{1}{2}}{1\frac{1}{2}}$

or $22 \times 150 = 3,300$ ft. lb. Hence, merely the weight in pounds multiplied by the number of climbs gives the work per minute.

Not only may one ascertain in this way whether an adult or child is fit to perform the average physical work for his sex, age, and weight, but one can learn, also, what is his actual physical capacity, be he invalid or athlete. The number of climbs that the subject is able to perform divided by the number he should be able to perform, according to the table, gives his percentage of efficiency. A few illustrative cases will make this clear.

CASE 1.—Mrs. A. R., aged fifty-three years, weight 156 pounds. Her diagnosis was chronic rheumatic valvular disease, mitral stenosis and insufficiency, an enlarged heart. The theoretical average number of ascents, for her age and weight, obtained from the table, is 17; but two tests were performed on May 22, 1931, the first of 14 ascents, and the second of 12. The resting figures were: blood pressure 130/96, heart rate 82 beats per minute. Two minutes after 14 ascents: blood pressure 140/96, heart rate 96 beats per minute. It is obvious that 14 climbs was too much, as the heart rate difference was fourteen whereas the extreme limit is ten. Later in the day, twelve climbs were essayed. The resting readings were: Blood pressure 150/100, heart rate 96 beats per minute. Two minutes after 12 ascents: blood pressure 146/96, heart rate 96 beats per minute. This last test was well performed, and hence her limit was between 12 and 14, that is, 13. In foot pounds this would be $13 \times 156 = 2,028$ ft. lb. In percentage of efficiency $\frac{13}{17}$, or 77 per cent.

The two-step test occasionally has given us evidence revealed by no other means at our disposal. The following case history is that of a man with a bad myocardium in whom for a long time the exercise tolerance was the only abnormal finding.

CASE 2.—Mr. R. P., aged fifty-two years, weight 149 pounds, sustained an acute coronary artery occlusion while in Miami, Florida, April, 1932. He had had an essential hypertension. I first saw the patient on June 30, 1932, and have followed

his case to the present time. The electrocardiogram, which during the April occlusion had revealed inversion of T_1 , on July 6, 1932 (Fig. 2A), disclosed slight R-T abnormalities. The patient did not complain, the physical examination was negative, and according to the x-ray film the heart and aorta were normal. The exercise tolerance test, however, showed only 14, whereas the normal for one of his weight and age is 21. His percentage of efficiency was, therefore, $\frac{14}{21}$ or 67 per cent. Because of this low exercise tolerance he was given a guarded prognosis and classed as totally disabled at the time. Although he retired from business and retained a trained nurse, he did not improve and suffered another acute coronary artery occlusion on July 8, 1933, from which he has only barely recovered.

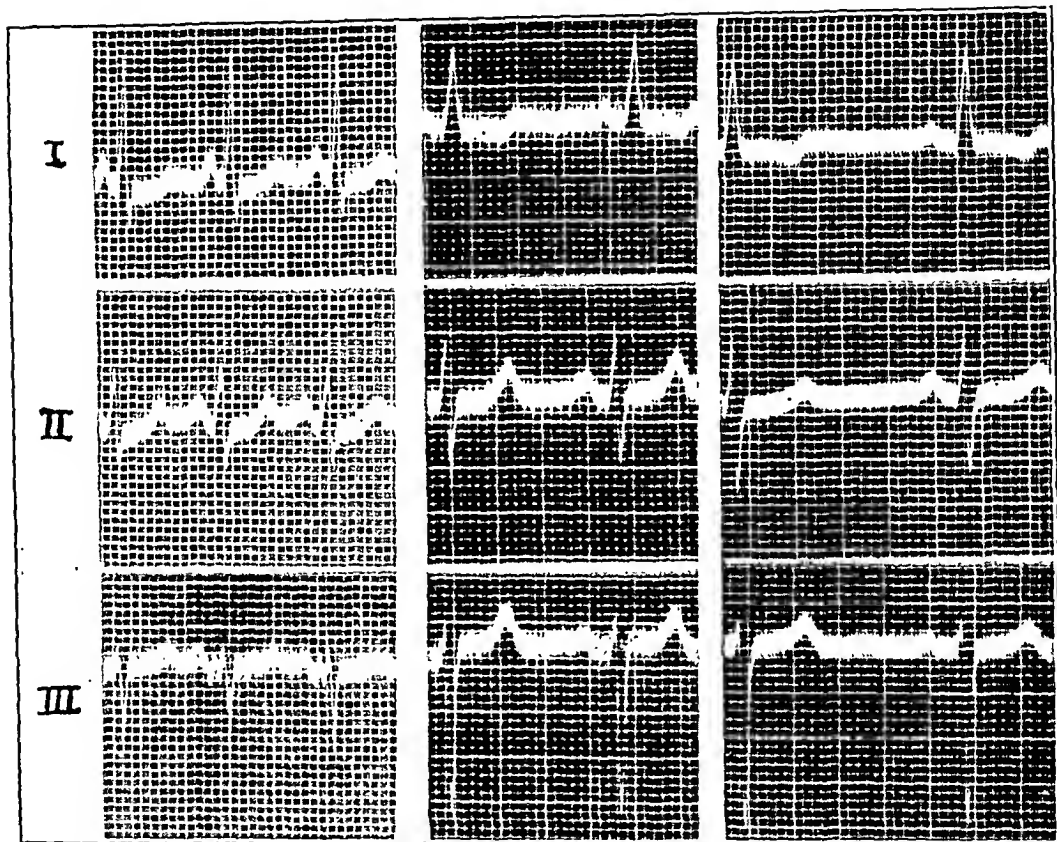


Fig. 2.—A, Case 2, Patient R. P., fifty-two years old. Although the electrocardiogram July 6, 1932, revealed only slight RS-T abnormalities, the exercise tolerance was poor and the percentage of efficiency was only 67. The patient developed an acute coronary artery occlusion July 8, 1933.

B and C, Case 3, Patient B. M., fifty-two years old. B, Electrocardiogram, June 22, 1931, disclosed definite T-wave inversion in Lead I, but the exercise tolerance was fairly good and the percentage of efficiency 86.

C, Electrocardiogram, February 15, 1934, the same. Exercise tolerance improved, percentage of efficiency 95. Patient still well.

Following is the story of a patient whose exercise tolerance test gave a truer picture of his cardiac condition than did his definitely abnormal electrocardiogram and one which the history of his case would not lead one to suspect.

CASE 3.—Mr. B. M., also fifty-two years old, was first observed by me on April 7, 1931, a few months after he was said to have had an acute coronary artery occlusion. He had weighed 230 pounds before this episode, but his weight at the time of observation was 179 pounds. The patient was taking digitalis and was working. Although he was advised to discontinue the digitalis and to stop work, he did neither. April

14, 1931, he sustained another severe acute coronary artery occlusion. For twelve weeks he was in bed, very ill. His diet was kept at a minimum so that when he was permitted out of bed he weighed only 150 pounds. His electrocardiogram, March, 1932, (Fig. 2*B*) showed the T-wave in Lead I to be definitely inverted and the QRS waves to be slurred. The patient's exercise tolerance on that date was 18, which was fairly good; efficiency was $\frac{18}{21}$ or 86 per cent. His prognosis was, therefore, considered good. Although the electrocardiographic picture has remained absolutely unchanged to date (Fig. 2*C*), his exercise tolerance has improved. By December, 1932, it was: $20 \times 150 = 3,000$ ft. lb. or $\frac{20}{21} = 95$ per cent efficiency. Because of this good exercise tolerance and despite the same definitely abnormal indications of the electrocardiogram, the patient was permitted to return to his regular work, as a sugar broker. For the last fourteen months he has worked as hard as he did before he became ill, has had no complaint and looks better than he ever did. The exercise tolerance in February, 1934, was absolutely normal, that is, 21 ascents.

One of the most difficult questions to answer is that of a patient when he asks, "How much work may I do?" The exercise tolerance test is of distinct aid in making a wise reply. The test is an objective method and serves to distinguish the neurasthenic or malingerer from the truly incapacitated.

It has been suggested that a patient's work capacity probably varies from day to day, but those using the test have been impressed with the uniformity of the number of ascents for an individual. Thus, if one's limit is 25 climbs today, it will be that tomorrow and probably weeks and months later, provided the weight remains approximately unchanged. If he tries 26 climbs, he will fail to do this. Examples will demonstrate these principles.

On November 14, 1926, the "two-step" test was performed by a man thirty-one years of age, weighing 157 pounds and 5 ft. 10 in. in height. This person was then in exceptionally fine physical condition as a result of handball playing, swimming in indoor pools, etc. It is not surprising, then, that he was able to perform an unusual number of climbs, namely 33.

	TIME	BLOOD PRESSURE	PULSE
Final resting figures		120/76	62
Exercise started	11:57:00 A.M.		
Exercise ended (33 climbs)	11:58:30		
	11:59:00	200/78	118
	11:59:35	140/78	76
	11:59:55	136/76	72
Two minutes after exercise	12:00:30	124/78	64

Although this man was much more dyspneic than the average individual who performs less climbs, his blood pressure and pulse rate returned to within ten points of resting figures.

Nearly eight years later, May 17, 1934, the test was repeated on the same man who was now thirty-nine years of age and weighed 162 pounds.

	BLOOD PRESSURE	PULSE
	126/86	76
	118/86	72
	118/84	68
Resting figures	118/84	68
Two minutes after 26 climbs	132/84	68

It is evident that 26 climbs exceeded the man's limit, as the difference between the resting systolic blood pressure and that two minutes after exercise was more than ten. On June 5, 1934, the test was again performed.

	BLOOD PRESSURE	PULSE
	110/82	80
	108/84	80
Resting figures	108/82	80
Two minutes after 25 climbs	118/78	80

It was, therefore, concluded that this man could perform 25 climbs and no more. This conclusion was borne out by further observations on June 6, 1934, at 9:50 A.M. as follows:

	BLOOD PRESSURE	PULSE
	114/78	76
	114/76	72
Resting figures	112/76	72
Two minutes after 26 climbs	126/78	80

Again 26 had been too much. The test, repeated at 12:18 P.M., disclosed, as usual, that 25 could be performed.

	BLOOD PRESSURE	PULSE
	114/84	64
	114/82	68
	112/80	68
Resting figures	112/80	68
Two minutes after 25 climbs	118/78	68

It has been mentioned already that Barringer¹⁸ observed that his results varied only slightly from day to day in the same individual. The present observations corroborate his conclusion. This invariability makes the two-step test dependable.

COMMENT

Not only does clinical experience seem to demonstrate that the two-step test is a measure of myocardial capacity, but when one turns to the mathematical formulas, established by the physiologists, for the work performed by the heart, one observes that this work is directly related to the mean arterial pressure and the pulse rate which have been used as factors in the present test. In 1895, Frank²⁹ published the formula $A = PV + (1/2 mv^2)$, in which A represents the work of the heart, P , the mean arterial pressure of the aorta, and V , the volume of blood ejected at each heartbeat, ($m =$ the mass of ejected blood, and $v =$ its velocity). The mean arterial pressure of the aorta is related directly to the systolic and diastolic blood pressure, and the work per minute is, therefore, the work per cardiac contraction multiplied by the pulse rate. Evans and Matsuoka,³⁰ Tigerstedt,³¹ and Wiggers³² have used the same formulas as Frank; the first half of the equation representing the work of the heart in overcoming arterial resistance and the second, the kinetic energy imparted to the blood to move it along. The former, PV , in which the blood pressure appears is considered to be 90 to 99 per cent of the work of the heart in human beings. This appreciation that the work of the heart per minute is a function of the systolic and diastolic blood pressures and the pulse rate has led Barach³³ to use these three figures as an "index" of the functional capacity of the heart. He cited the formula S. D. R. in which the systolic and diastolic blood pressures were added and then

multiplied by the rate of the heart. This formula, of course, did not give the quantitative measurement of the work of the heart, and here the criticism applied to previous tests again is pertinent, namely, that no standard measurements have been constructed for normal people. The study of these formulas, nevertheless, proves that when considering the factors of blood pressure and heart rate one is concerned with figures directly related to the work of the heart. In the present test all three of these factors are utilized. Hence, for these reasons and from clinical experience, it is thought that the two-step exercise is a measure of "myocardial function."

The influence of a man's occupation and physical training has been noted. Whether a man be a sedentary worker, such as a bookkeeper, or an outdoor salesman, the number of climbs is in the usual normal range. In the case, however, of a man in strenuous physical training, such as a student on the football squad, it will be found that his limit is beyond the figures given in the table.

In the "two-step" test the systolic and diastolic blood pressures, measured by the auscultatory method, and the pulse rate have all been used. Each of these, two minutes after completion of the exercise, must return to within ten points of the resting figures. It has been observed in patients in whom this does not occur that it is usually the systolic blood pressure that does not return to "basal" figures. The pulse rate is next in frequency of nonreturn, and the diastolic blood pressure is found to vary least. Schellong³⁴ obtained similar results. This feature was brought out in the first test of the man whose exercise tolerance was reviewed eight years later. It would appear that when work is demanded of the heart the systolic blood pressure is first altered, then the pulse rate, and last the diastolic pressure. These statements have more than mere academic or even physiological interest, for they mean that the number of climbs accomplished do not "strain" the heart even temporarily. If normal persons are asked to perform many more climbs than are called for in the tables, there will be a delay of three, four, five, or six minutes before the readings return to resting levels. This has been shown by the many authors referred to earlier in the paper.

After considerable experimentation, a short duration of exercise, such as one and one-half minutes, had been found most useful. The same numeral, one and one-half, for the height of the steps simplifies the mathematical process in calculating the foot pounds of work performed. This has already been demonstrated in the present text, but these matters were more fully discussed in the article published in 1929.²⁸ An extensive experience seems to prove the advisability of this short and nonstrenuous form of exercise since no untoward accidents have ever occurred. In more than 100 cases of anginal syndrome

we have never observed a single onset of pain. Undoubtedly, had the rate of climb been accelerated or the duration of climb been increased, pain would have been elicited. In the average patient observed in office or clinic the test produces only slight fatigue and but moderate dyspnea. In fact, most patients have an inclination to perform more climbs than the number required. The two-step climbing test, therefore, meets all the requirements laid down by White³⁵ when he said, "A simple test is less apt to strain unaccustomed muscles of the subject, less apt to exhaust prematurely a person not in good physical

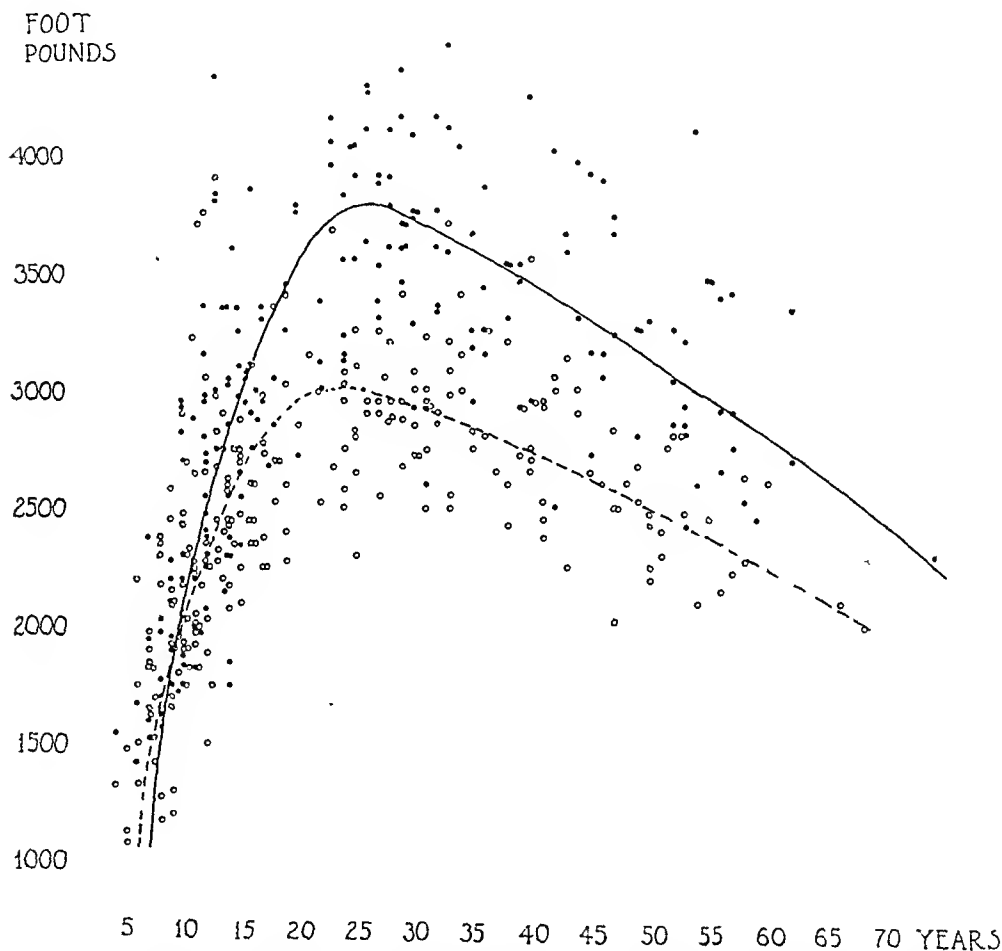


Fig. 3.—Relation of age to exercise tolerance as expressed in foot pounds of work per minute. Straight line (through dots) for male and broken line (through circles) for female individuals.

training and more convenient and practical to execute. In fact, such simple exertion as enters into the routine daily life of the patient is best of all."

The number of ascents itself is an index of physical efficiency and a consideration of "percentage" of efficiency is not essential, for foot pounds of work per minute, as has already been shown, is the number of climbs multiplied by the patient's weight. However, per unit of weight, that is per pound of the patient, this number would be divided

by the patient's weight, the result again being the number of ascents. Hence a patient's efficiency can be judged directly by his limit in climbs.

Up to the age of ten or eleven years, both boys and girls show a very rapid increase in number of foot pounds of work per minute. (Fig. 3.) There is a slowing down of this rapid ascent in females and the maximum of about 3,000 ft. lb. is reached between the ages of twenty and twenty-seven years. In men, however, a rapidly increasing capacity for work continues practically unabated until the age of twenty-two years, and between twenty-two and thirty-one years

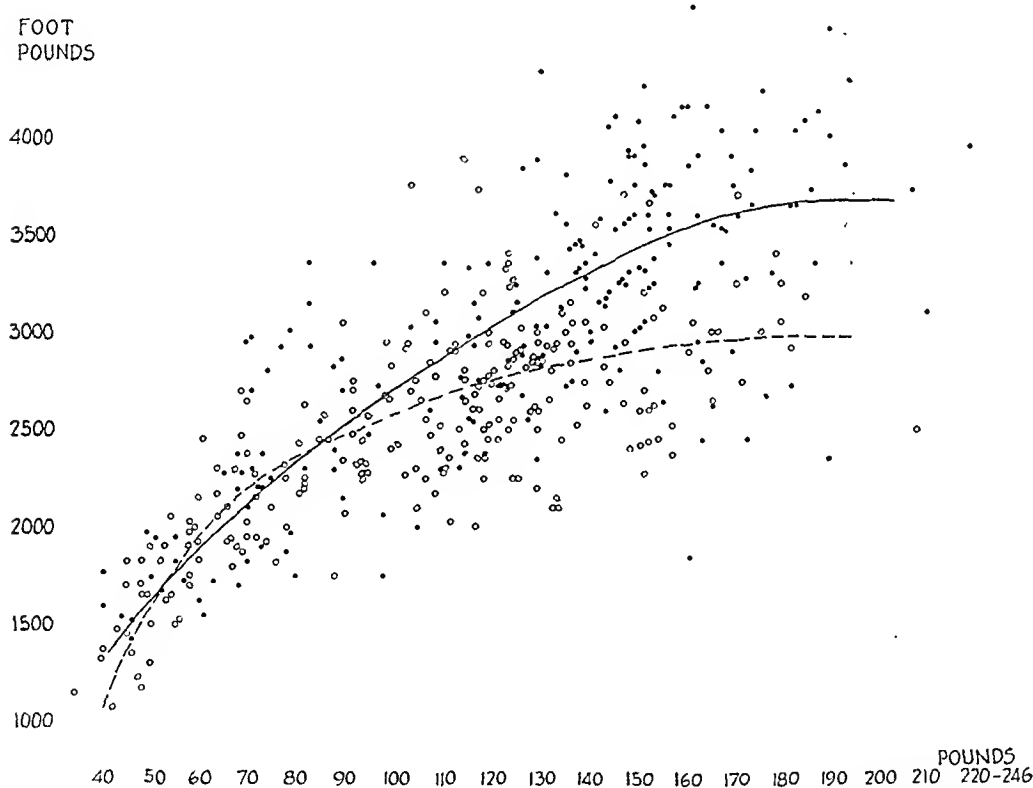


Fig. 4.—Relation of weight to foot pounds of work performed per minute. Straight line for male and broken line for female individuals.

the maximum of about 3,800 ft. lb. is reached. With advancing age, in both sexes, there is a steady, progressive decline in work capacity.

In general, the foot pounds of work performed increase rapidly with greater weight, until seventy to ninety pounds is reached. (Fig. 4.) The slope then becomes more gradual in the case of women. In men the slope is hardly changed, the maximum work is most often attained when men weigh 170 to 200 pounds and when women weigh 150 to 180 pounds. Men are capable of performing more work per weight, the maximum for men being about 3,700 ft. lb. of work per minute, for women about 3,000 ft. lb. of work per minute.

The test offers an unusual means of research. By it, one can classify quantitatively the myocardial reserve of patients with valvular disease. How do patients with mitral and those with aortic lesions compare? Does the exercise tolerance correspond to the heart size rather than to the valvular lesion? What are the quantitative limits of patients with an anginal syndrome, essential hypertension, exophthalmic goiter? Recovery from acute disease may be investigated. Occasionally, patients have complaints for as long as three to six months after an acute lobar pneumonia, of dyspnea on slightest exertion, fatigability, weakness, or rapid pulse, and in them the exercise tolerance has been found below normal. Simultaneously, with increase in work capacity, as indicated by the two-step test, the symptoms have disappeared. Frequently in a patient with an anginal syndrome the exercise tolerance has been the only objective evidence of myocardial impairment. In the malingerer it is normal.

It has been pointed out to me that the number and extent of the respiratory excursions are not considered in this test. This is a just criticism, but as three factors already are considered, namely, systolic blood pressure, diastolic blood pressure and pulse rate, it has seemed best not to complicate it by the addition of a fourth variable.

Precautions to Be Observed Before Test Is Performed.—A question that must and does arise is that of the lability and variability of the blood pressure and pulse rate. As excitement, emotion, and apprehension affect them, naturally, correct readings cannot be obtained when these influences are at play. I always find some means of having the patient rest comfortably, at least for five minutes, before blood pressure and pulse rate are recorded. Readings are repeated until the lowest is ascertained. It will be found that a basal or resting blood pressure and pulse rate exist in individuals just as there is a basal metabolic rate. It seems to make no difference whether the "resting" readings are taken in the sitting or in the lying position, provided the patient returns to the same position after the exercise.

Before the patient begins the ascents, the examiner demonstrates how the test is performed. The patient is assured that he is not to run, that he may gain support, or reassurance, by lightly placing one hand against the wall, and, in fact, the examiner may gently support the moderately sick patient by taking hold of one arm lightly, as the patient climbs the steps. As long as he is not given a vertical lift, this support does not interfere with the work which he performs.

There are other precautions which are important. Certain drugs lower the exercise tolerance. This applies to an individual who is receiving thyroid extract, or ephedrine, or who is taking alcoholic intoxicants or smoking excessively. Even one or two cigarettes smoked immediately before the test will have this effect. An acute upper respiratory infection, like a coryza, pharyngitis, tracheitis, sinusitis,

will show a similar lowering in limit of ascents. No special investigation of women during the menstrual cycle has been undertaken, but it has been observed that this affected the test in one woman. In two cases diagnosed as neurocirculatory asthenia the test showed the limit to be below average. In these people it may be, as White³⁶ has suggested, that the test is a measure of the "fitness of the nervous system" but this is a debatable question. It may be that in a person with effort syndrome the myocardial reserve is limited.

SUMMARY

A simple quantitative "two-step" test of myocardial function is described, and tables of climbs are given for normal individuals, from four to seventy-four years of age, of both sexes. The patient's weight multiplied by the number of ascents gives the foot pounds of work per minute. Not only may it be learned in this way whether the exercise tolerance of an individual is within average figures, but his actual limit may be ascertained. The percentage of efficiency is calculated by dividing the number of climbs the patient can actually perform by his theoretical limit, as derived from the tables.

Men have greater exercise tolerance than women. The maximum of this tolerance appears to be about 3,800 foot pounds of work, in men between twenty-two and thirty-one years of age weighing from 170 to 200 pounds. The maximum for women appears to be 3,000 foot pounds of work performed between the ages of twenty and twenty-seven by individuals whose weight is about 150 to 180 pounds. Older and heavier men and women show a decline in exercise tolerance. Children show the greatest efficiency, that is, the number of ascents possible in the given time is highest in the young. There is a sharp rise until puberty, then the slope is more gradual until the twenties are reached.

Thyroid extract, ephedrine, alcohol, excessive smoking, and upper respiratory infections affect the results.

The test is a definite aid in the diagnosis and evaluation of cardiovascular disease and in deciding how much work, or sport, or other activity the patient may be permitted. It also helps to differentiate functional and organic disease of the heart and is particularly useful in the anginal syndrome.

The measure of exercise tolerance determined by the two-step test is a fairly constant figure from day to day, and, unless one is in athletic training, similar results are common in those who lead a sedentary and those who live an outdoor life.

The exercise tolerance test may be the only objective evidence that the myocardium is involved.

The exercise test is not a strain, and no untoward results, even in cases of anginal syndrome, have ever been observed.

Clinical experience, mathematical deduction, and physiological reasoning appear to prove that the test is an index of myocardial function.

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THE CIRCULATORY RESPONSE TO EXERCISE IN PATIENTS WITH ANGINA PECTORIS*†

THERAPEUTIC IMPLICATIONS

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STUDIES of the pathological and clinical findings in patients with angina pectoris, begun by Jenner¹ in Heberden's time and continued to the present, have yet to establish a constant or predictable relationship, except in the instance of coronary thrombosis, between what is observed clinically and what is found on post-mortem examination. Coronary sclerosis is believed to be quite intimately connected with angina pectoris. It is well known, however, that sometimes even the most advanced cases of coronary arteriosclerosis are associated with no clinical phenomena whatever. Mönckeberg's² studies of the coronary arteries in the fatalities in the Great War showed that in 652 autopsies coronary arteriosclerosis was found in 353; similar observations were made by Rössle.³ One is therefore tempted to conclude, as does the pathologist Aschoff⁴ in remarking on the fact that angina pectoris has been observed where no coronary sclerosis was present, "that purely functional factors may be responsible for the genesis of the disease." Such inconsistencies between pathological and clinical observations would make it appear that perhaps the important differences between patients with angina pectoris and individuals in the same age group with no clinical evidence of heart disease might be more manifestly physiological than pathological.

Since angina pectoris is characterized by the development of pain on exertion, we have attempted to determine what happens during exertion in patients who suffer from angina pectoris which differs from what is known to occur in those who do not have angina pectoris. We refer, of course, to the so-called angina of effort. We have been unable to find any account of observations on patients with angina pectoris during exercise, although it is under such conditions that we should expect to find the chief differences between such patients and normal people. Wayne and Laplace⁵ have recently recorded observations made immediately before and after attacks of angina pectoris induced by stair climbing. In this study the physiological events preceding and perhaps responsible for the attack were not observed. This was

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DATA CONCERNING PATIENTS WITH ANGINA PECTORIS

PATIENT	AGE	SEX	HEIGHT	WEIGHT	BLOOD PRESSURE	DURATION	HEART SIZE	ELECTROCARDIOGRAM	REACTION TO EXERCISE*	COMMENT
L. N.	64	M	5' 5"	154	160/90	2.5 yr.	Mod. enlarged	Left axis deviation	I	Thyroidectomy 10/28/33.
B. A.	61	M	5' 6"	171	120/90	2 yr.	Mod. enlarged	Left axis deviation	I	
A. W.	68	F	5' 3"	127	170/86	4 mo.	Normal	Left axis deviation with sharply inverted T _{2,3} and deep S ₂	I	
I. S.	64	M	5' 5"	175	106/75	2 yr.	Mod. enlarged	Inverted T _{1,2} with left axis deviation	I	Thyroidectomy 9/29/33. Probably coronary occlusion 10/13/33.
O. H.	68	M	5' 4"	165	155/95	3 yr.	Mod. enlarged	P-R 0.21 sec. Inverted T ₁ . Low complexes	I	Thyroidectomy November, 1933.
T. C.	64	M	5' 10"	169	160/90	1.5 yr.	Mod. enlarged	Left axis deviation	I	Thyroidectomy 11/22/33. Probably coronary occlusion Nov., 1932. Def. cor. occ. April, 1934.
C. E. C.	72	M	5' 6"	155	118/73	3 yr.	Mod. enlarged	Left axis deviation with auricular extrasystoles	II	Onset with probable cor. occlusion in 1929.
L. K.	52	M	5' 5"	170	170/110	2 yr.	Mod. enlarged	Left axis deviation T _{1,2,3} erect. S ₂ deep	II	
E. L.	71	M	5' 9"	188	170/100	5 yr.	Markedly enlarged	Normal axis with vent. extrasystoles	III	
E. F.	60	M	5' 8"	165	175/115	2 yr.	Normal	Left axis deviation. Inverted T ₁	III	Probable coronary occlusion 1/3/33.
P. W.	74	M	5' 6"	145	160/90	14 yr.	Mod. enlarged	Left axis deviation. T _{1,2} inverted. Deep Q ₃	III	
M. S.	44	M	5' 6"	131	145/85	4 yr.	Normal	Left axis deviation with low T ₁ . Erect T _{2,3}	IV	
C. J. E.	63	M	6'	208	170/100	15 mo.	Mod. enlarged	Normal	IV	Onset with coronary occlusion Jan., 1932.
L. H.	67	M	5' 7"	138	165/102	2 wk.	Mod. enlarged	Normal	IV	
J. C.	54	M	5' 6"	166	150/84	2 yr.	Sl. enlarged	Normal	IV	
P. A.	43	M	5' 4"	150	86/64	1 yr.	Normal	Left axis deviation. Coronary T ₁	V	
L. G.	52	M	5' 3"	165	138/84	2 mo.	Normal	Left axis deviation. T-waves erect S ₂ deep		

*Represents group classification referred to in the paper.

also true of the studies of Wood, Wolferth and Livezey⁶ who observed electrocardiographic changes during attacks of angina pectoris; and of Bischoff.⁷ Levine, Ernstene and Jacobson⁸ noted changes occurring in pulse, blood pressure, and electrocardiogram before, during, and after induced attacks of angina pectoris; but these attacks were initiated by injections of adrenalin, and one cannot assume that the circulatory response to adrenalin corresponds to the response to effort. The mechanism of the induction of pain under the two circumstances may well be entirely different.

Seventeen patients with angina pectoris, sixteen male and one female, have been studied. Six normal subjects in the same age group served as controls. The ages ranged between forty-three and seventy-two years. In all patients the history was obtained of substernal pain brought on by exertion, relieved by rest. All patients were excluded where there was even the slightest doubt that they represented typical cases of angina of effort. The duration of angina pectoris in all cases, except two, was more than one year; in three patients there was a past history suggesting coronary thrombosis. Further pertinent data concerning the patients with angina pectoris are summarized in Table I.

METHOD

Observations were made at the same time of the day under the same conditions. Before exercise was begun, with the patient sitting quietly on a stationary bicycle, the blood pressure, pulse rate, respiratory rate, and respiratory minute volume were obtained. The patient then pedalled at a slow rate (fixed by metronome) and with a four-pound pull (185 kg. M. work per minute) for three minutes. During the exercise the number of heartbeats was recorded for each ten seconds. This was made possible through the use of a small portable cardiotaehometer designed and constructed by V. Guillemin of Massachusetts Institute of Technology. Also, during exercise the blood pressure, respiratory rate, respiratory minute volume, and oxygen consumption were obtained for each minute. Immediately after exercise we continued to count the heartbeats in ten-second periods, and we recorded the blood pressure at intervals of one minute. Oxygen debt was measured for a ten-minute period. With such short and light exercise we found that at the end of ten minutes following the cessation of exercise the oxygen consumption had practically reached its pre-exercise level. Oxygen consumption was measured using the open circuit method, the air samples being analyzed in a standard Haldane apparatus.

To determine capacity for work without pain we allowed the patients to pedal at a fairly rapid rate and with a six-pound pull (395 kg. M. work per minute) until the first evidence of cardiac pain developed, at which point the exercise was stopped.

RESULTS

General.—There were four general types of response, the most striking disturbance in these groups being (1) failure of pulse rate to rise normally during exercise; this was accompanied by normal respiratory response; (2) the development of cardiac irregularity (extra-systoles) shortly before the onset of pain and its disappearance shortly after the cessation of exercise (the response of the cardiac rate, blood pressure and respiration was normal in these cases); (3) a thin, rapid, barely palpable pulse during exercise which became full and strong

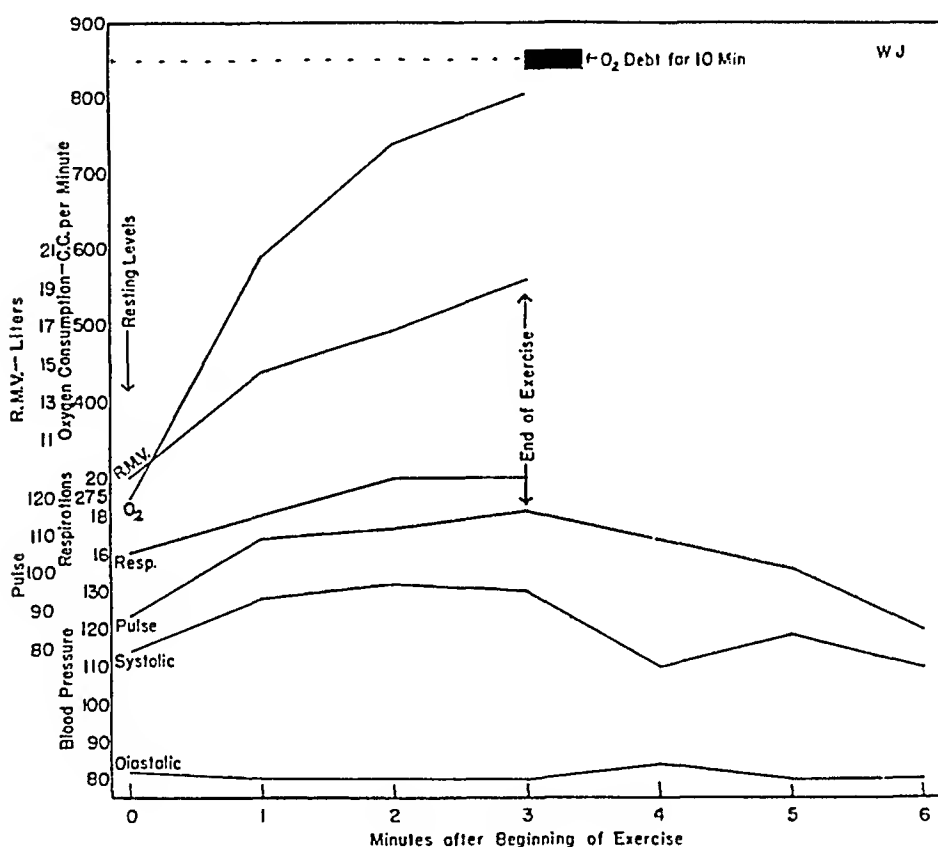


Fig. 1.

again shortly after the cessation of exercise (frequently, the pulse could not be palpated during exercise in these cases); associated with this pulse phenomenon in exercise was a low pulse pressure; (4) primary respiratory distress with rapid pulse rate, the type of response characteristically associated with cardiac weakness.

Normal Response.—The response of only one of the normal subjects is described, since it is typical of what occurred in the others. In this case (cf. Fig. 1) the respirations increased from 16 to 20 per minute, the respiratory minute volume from 9.0 to 19.3 liters per minute, and the pulse rate rose from 88 to 109 during the first, 111 during the second, and 116 during the third minute of exercise. In the third

minute after exercise it was back to 85. The oxygen consumption rose from 270 c.c. per minute before exercise to 587 c.c. per minute during the first, 738 c.c. per minute during the second, and 804 c.c. per minute during the third minute of exercise. There was an oxygen debt of 850 c.c. The blood pressure is seen to rise from 114/82 mm. Hg before exercise to 130/80 mm. Hg in the third minute of exercise. It dropped quickly after exercise to its resting level.

There was thus a slow rise in the respiratory rate, a moderate increase in pulmonary ventilation and pulse rate and a moderate rise in the oxygen consumption which in the second minute of exercise was within 10 per cent of what it was in the third. The blood pressure rose, as was to be expected, chiefly in the systolic phase so that the pulse pressure was increased. The pulse was easily palpable during the exercise.

RESPONSE IN PATIENTS WITH ANGINA PECTORIS

Failure of Pulse Rate to Rise Considerably.—In six of the patients the pulse rate failed to rise, during exercise, to the normal level. In these cases the pulse rate during exercise did not exceed 90 per minute whereas the normal rise under the conditions of our experiments was to 110 to 120 per minute. In one case the rise was from 53 to only 66 per minute. Usually the rate during exercise in this group was between 75 and 85. These are rates recorded during the first experimental period without preliminary training. In most of the cases the experiment was repeated several times. The pulse rate, instead of becoming still slower, as might be expected, either was unchanged or rose slightly. The typical response to exercise in one of the patients in this group is seen in Fig. 2. There was practically no rise in respiratory rate, the pulmonary ventilation increased somewhat, the pulse rate rose only from 60 to 81 per minute, and was 63 in the first and 58 in the second minute after exercise. The oxygen consumption rose normally, being practically the same in the second and third minutes of exercise. The oxygen debt was 520 c.c. The blood pressure did not change considerably during exercise except for a slight rise in the diastolic pressure. However, immediately after the exercise was finished, the systolic pressure rose and returned in two minutes to the level before exercise. This failure of the blood pressure (usually systolic and diastolic, occasionally only systolic) to rise during exercise was noted in two of the other three patients in this group in whom the blood pressure could be measured during exercise. In one of these patients, for example, the blood pressure before exercise was 120/80 mm. Hg; during the third minute of exercise it was 120/80 mm. Hg; in the first minute after exercise it had risen to 152/90 mm. Hg; and it remained at this level for three minutes. In the other patient in this group the blood pressure was 142/76 mm. Hg

before exercise; 142/84 mm. Hg in the third minute of exercise; 158/70 mm. Hg in the first minute after exercise; 152/78 mm. Hg in the second minute and 142/72 mm. Hg in the third minute after exercise.

The failure of the blood pressure to rise during exercise was followed by a definite rise immediately after exercise. This type of blood pressure response was noted in only one of the other patients. Wayne and Laplace⁵ noted in some of their patients a rise in blood pressure after an attack of pain had been induced by stair climbing. Although pain was not produced in our cases, it is likely that we are here dealing with the same type of response to mild exercise. Cotton, Rapport and Lewis⁹ observed a similar rise in blood pressure after

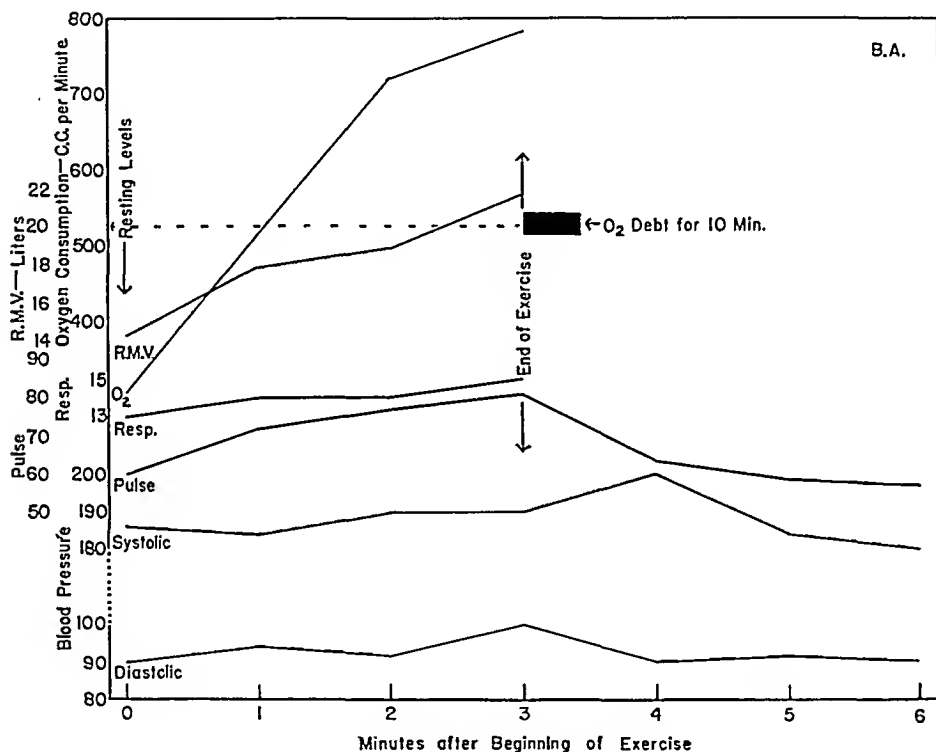


Fig. 2.

the end of exercise in some normal subjects. However, in most of these cases there was evidence of some rise in blood pressure during exercise also.

Failure of the pulse rate to rise during exercise is an interesting phenomenon capable of various interpretations. In this connection it is interesting to recall some of the clinical observations made during attacks of angina pectoris by students of the disease. Osler remarked, "Considering the increase in the respirations and the congestive state of the face and the neck, I was surprised that the pulse changed so little."¹⁰ In Maekenzie's writings is recorded the following statement: "That attacks of great severity may be accompanied by no change in the heart action is, I think, beyond doubt."¹¹ Allbutt,

who apparently was intrigued by the frequent observation of the slow pulse rate during attacks of angina pectoris, graphically and in characteristic vein reminds us that "amid the agitation of patient and attendant, the heart, assumed to be the protagonist in the conflict, often seems to be the one impassive actor."¹²

Apparently the patients referred to in these quotations are in the same functional class as those under observation in this group. Occasionally, during experiments on patients in this group, cardiac pain supervened, and we found that the pulse rate remained slow. This was found to be true, also, on several occasions when some of the patients in this group were allowed to exercise until pain developed. We may, therefore, state that those patients in whom a slow pulse rate is noted during an attack probably have an abnormally slow rate during the exertion preceding and initiating the attack.

Can this slow cardiac rate in any way be responsible for the attack? Rein¹³ by the use of his "stromuhr" showed that for a given amount of work the total blood flow through the coronary vessels is related chiefly to the rate of the heart and not to stroke volume or the mean arterial pressure. Other conditions being equal, the minute flow of blood through the coronary vessels is greater when the cardiac rate is more rapid. The volume of blood which flows through the coronary vessels was found to be more greatly increased when the increased cardiac output was associated chiefly with an increase in cardiac rate than when this increase in cardiac output was largely due to an increase in stroke volume. Therefore, we may assume that in the patients under discussion, a failure of the pulse rate to increase considerably during exercise may entail a less adequate blood flow through the coronary vessels. And, if we assume that cardiac pain is the result of relative myocardial anoxemia, we may conclude that the failure, in these patients, of the pulse rate to rise during exercise perhaps is an important factor in the production of the anginal attack. If the pulse rate is slow because of increased vagal tone, then the added factor of coronary constriction^{14, 15} resulting therefrom might also assume some importance.

2. *Extrasystoles on Exertion.*—In two of the patients an irregular heart action developed on exertion which in one case was found by electrocardiogram to be due to auricular and in the other to ventricular extrasystoles. The general response to exercise in these two patients was otherwise not unusual. There was no abnormal response of the respiratory rate, pulmonary ventilation, or oxygen consumption. The pulse rate did not rise considerably in the case of L.K., although the rate during exercise was not considered slow enough to place this patient in the preceding group. In the case of C.E.C. the type of blood pressure response above referred to, namely a failure to rise except after exercise, was noted.

In both these cases exercise tolerance tests were performed, that is, the patients were asked to pedal at a fairly rapid rate against a pull of six pounds (395 kg. work per minute) until they experienced pain. In this manner under fixed conditions we found that on four occasions in the case of C.E.C. (cf. Fig. 3) the irregularity developed at about the same time before the onset of pain and remained for about the same time afterward. The level of the cardiac rate at which the pain developed was somewhat variable. In the other patient, L.K., these same conditions obtained, the irregularity occurring 40 to 85 seconds before the onset of pain and disappearing 30 to 70 seconds after the cessa-

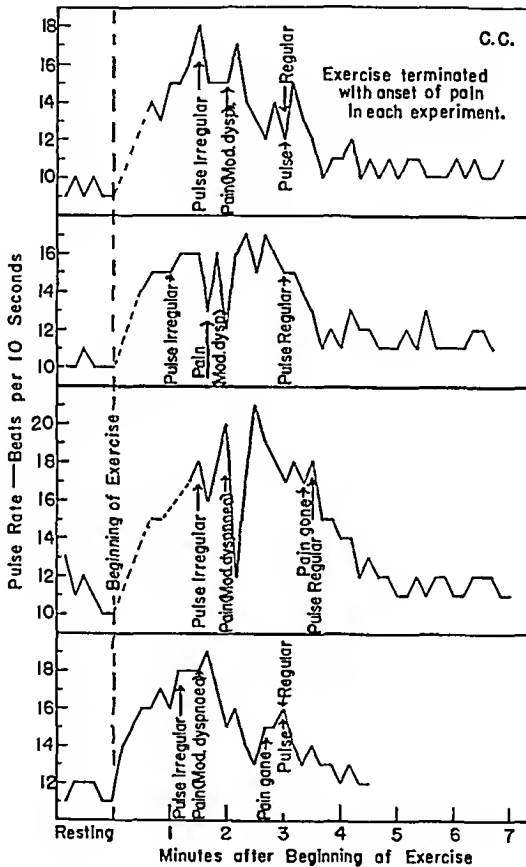


Fig. 3.

tion of exercise and after the pain had subsided or disappeared. The patients did not ride until the pain was fully developed but rather until they had the first intimation that pain was coming on. For this reason the duration of the pain was short. We were able to confirm the observations of Wayne and Laplace⁵ and of Blumgart, Riseman, Davis and Berlin¹⁶ that under constant conditions cardiac pain is brought on by a fixed amount of work, fairly regularly in a given patient.* In some of the patients presented in other groups an occa-

*This was so striking that in several patients this fact has been helpful in the diagnosis of true angina pectoris. In such cases nitroglycerin invariably increased capacity for work, whereas a saline tablet used as a control would have no effect.

sional extrasystole was found to be present in an inconstant manner after exercise or after an attack of pain. These patients, because they exhibited only rare extrasystoles and those inconstantly, are not considered in this group. In one patient, however, frequent extrasystoles were observed before, during, and after exercise, the irregularity being usually less marked during exercise. This patient will be included in this group in the discussion below devoted to therapeutic results. Wayne and Laplace noticed occasional extrasystoles at rest in a few of their patients with angina pectoris. In some they found extrasystoles when the pulse rate was approaching its normal level after exercise and often before the pain had passed off. It is quite possible that had observations been made during the exercise preceding the pain on those patients in whom extrasystoles were noticed before the pain had passed off, a relationship of the extrasystoles to the pain would have been observed similar to that recorded in our patients. Goldhammer and Scherf¹⁷ noticed ventricular extrasystoles electrocardiographically during attacks of angina pectoris. Allbutt quotes A. Morison as observing during an attack of angina pectoris that "the pulse was not quickened but during the pain it occasionally intermitted."¹⁸ Mackenzie¹⁹ obtained pulse tracings during an attack which showed extrasystoles. In another case of angina pectoris Mackenzie found the heart to be "very irregular in action due to groups of idioventricular beats. It was difficult to correlate the irregularity with the attacks of pain as he was not always aware that his heart was irregular, but it was fairly evident that the pain came on with exertion when the heart was irregular."²⁰ Another patient of Mackenzie's observed that his attacks occurred only when his heart became irregular. He was conscious of the irregularity.²¹

It is possible that the irregularity is in some way responsible for the precipitation of the pain if we accept the view that the pain is due to myocardial anoxemia as a result of coronary insufficiency. We should also have to assume, as we may, reasonably, that the coronary flow is impaired in the presence of extrasystoles. We are inclined to the belief, as are Goldhammer and Scherf¹⁷ that the extrasystoles in these cases are in themselves evidence of myocardial damage, perhaps increased sensitivity from a relative ischemia. In such a case the extrasystoles would tend to increase the myocardial anoxemia, and the vicious circle would end in an attack of pain. Evidence is presented below to support such a view, for when the irregularity is abolished the heart can do much more work without pain.

3. *Thin, Rapid Pulse During Exercise.*—In three of the cases the pulse during exercise became rapid, thin, and frequently barely palpable. In these cases the pulse after exercise soon resumed the full

strong character which it had manifested before exercise. The pulse rate during exercise in these cases was over 120, usually 135 to 160 although the work was relatively light (185 kg. per minute). It is noteworthy that the pulse pressure during exercise in these cases either failed to increase significantly or became smaller. Thus, in the case of E.F. (cf. Fig. 4) the blood pressure before exercise was 230/120 mm. Hg with a pulse pressure of 110 mm. Hg. In the first minute of exercise the pulse pressure was 110 mm. Hg, in the second minute

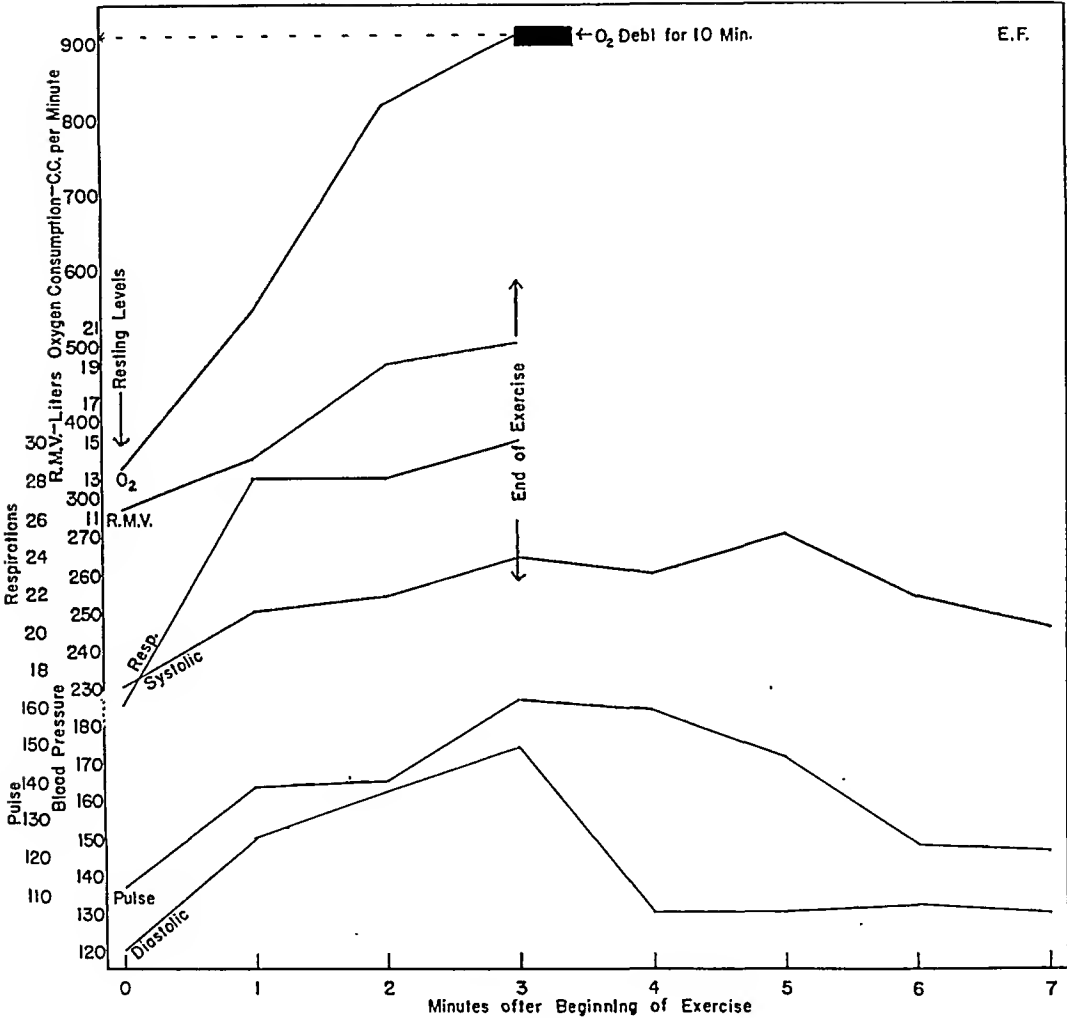


Fig. 4.

92 mm., and in the third minute 90 mm. Hg. In the first minute after exercise the pulse pressure arose to 130 mm. Hg and remained above 100 mm. during the next few minutes. The pulse rate which was rapid before exercise (112 per minute) rose to 162 during the exercise and four minutes after exercise was still 121. During exercise the pulse was frequently impalpable; at times it could barely be felt, being exceedingly thin. The oxygen consumption, pulmonary ventilation, and respiratory rates were normal during the exercise.

Perhaps it is this type of patient in whom an abnormal sensitivity exists to adrenalin as suggested by Levine, Cutler and Eppinger.²² The type of response might suggest excessive sympathetic stimulation, being accompanied as it is by such very rapid cardiac action. This rapid action might be taken to indicate that the heart muscle is working inefficiently, for as Starling and Visscher²³ showed, the heart uses less oxygen to do a given amount of work when the rate is slow than when it is rapid. Thus a rate which is too rapid may lead to relative myocardial anoxemia and pain. Rein¹³ demonstrated that for a given amount of work the coronary flow was greater when the heart rate was more rapid. The work of Starling and Visscher and of Rein might be interpreted together as indicating that as the internal work or energy expenditure of the heart is increased by an increase in heart rate, the blood flow through the coronary vessels is increased to meet this added demand for oxygen. There is thus no inconsistency in the assumption that myocardial anoxemia with resulting pain may be precipitated either because the heart rate cannot rise sufficiently (cf. group above) or because it rises too much. For, if it cannot rise adequately, the coronary blood flow and, therefore, the supply of oxygen to the myocardium do not increase sufficiently to take care of the added work of the myocardium. In this case the added work of the myocardium is due chiefly to the increased stroke volume rather than to an increased heart rate. On the other hand, if the rate is too rapid, the energy expenditure of the myocardium is so great that the coronary flow cannot be increased sufficiently to supply an adequate amount of oxygen. Thus, either an inability of the heart rate to rise adequately or a too great rise in cardiac rate may induce relative myocardial anoxemia. Therapy in either case should be directed toward obtaining a normal rate which teleologically might be assumed to be the ideal rate rather than one which is too slow or too rapid; this, of course, in addition to coronary dilatation, if that be possible. One might also speculate on the possible effect on the coronary flow of the failure of the pulse pressure to increase. Evidence in regard to the relationship of pulse pressure to coronary flow is, however, contradictory.^{13, 24}

Regardless of the theoretical implications of the reactions, the fact remains that in some patients with angina pectoris the pulse rate during exercise rises to an abnormally high level; in others to an abnormally low level. In order to observe such abnormal responses it is best to employ light exercise, or exercise of such severity that normally a moderate rise in heart rate (to about 110 per minute) occurs. Then abnormally high or low levels are easily distinguishable.

4. *Dyspnea Preceding Pain.*—In three of the patients there was a definite and abnormal amount of dyspnea during the exercise. In

one patient (G.G.E.), the most striking in this group, the respiratory rate at rest was 16 per minute, the respiratory minute volume 12.6 liters. In the first minute of exercise the respiratory rate had risen to 22, the respiratory minute volume to 24.6 liters, and in the second minute of the exercise the respiratory rate had reached 36 and respiratory minute volume 36.8 liters. In the next five seconds the patient developed cardiac pain and ceased pedalling. This patient was obviously markedly dyspneic before the onset of the pain. (Pulse rate had reached 138.) Despite this, careful inquiry before the test had revealed no story of dyspnea in any way associated with his pains, and in response to a question after the test he replied that he had experienced no dyspnea. This case illustrates the inadequacy of simple inquiry in regard to information concerning the association of dyspnea with cardiac pain.

A second patient in this group, however, had noticed that he was definitely "winded" before he developed pain. In the third case, the history was indefinite.

In the two patients in this group in whom we were able to determine the oxygen consumption for the full three-minute period there was a slight delay in the increase of oxygen consumption during exercise and subsequently a somewhat greater oxygen debt (L.H. O₂ at rest 266 c.e. per minute, during first minute of exercise 300 c.e., during the second minute 527 c.e., and during the third minute of exercise 777 c.e. The oxygen debt was 1,100 c.e.). This is the type of reaction associated with cardiac weakness.^{25, 26, 27}

We interpret these findings as indicating that there is primary cardiac weakness which leads to general anoxemia on exertion manifested by breathlessness which in turn leads to local myocardial anoxemia and pain. Perhaps the pain prevents too much exertion and thus too early heart failure in this group.

5. *Normal Response.*—In two of the patients the response to exercise was the same as in the normal subjects. In these cases perhaps features of the circulatory response which we did not study might have been found to vary from the normal.

Discussion of Results.—It seemed to us not so important that there were the specific groups which we have outlined as that in a relatively small number of cases so many different types of reactions should have been observed. More cases will undoubtedly reveal even more types of response.

Thus, from another angle we are once more forced to the viewpoint that angina pectoris, even the angina of effort, is merely a symptom which may be a manifestation in different people of widely different disturbances. Given a patient with the symptom of cardiac pain on exertion, it is desirable to determine what type of circulatory disturb-

ance that patient has and to attempt to direct therapy toward correcting that disturbance. Even if we assume the pain of the angina pectoris of effort always to be due to relative myocardial anoxemia, there is no reason why various factors may not produce such a state.

THERAPEUTIC INDICATIONS IN THE VARIOUS TYPES OF RESPONSES

In that group of patients in whom the pulse rate failed to rise adequately during exercise it seemed likely that we might expect some benefit from the use of atropine since atropine not only raises the resting pulse rate but allows a pulse rate to reach a higher level during a given exercise without a concomitant increase in the level of oxygen consumption for that exercise.²⁸ In one patient in this group on whom frequent observations were made after careful control we found that there was no increase in capacity for work when atropine was administered in doses (1 mg. subcutaneously) large enough to produce a greater rise in pulse rate during exercise than in the control period. In another patient the capacity for work without pain was perhaps slightly diminished. This patient, however, had frequent extrasystoles before and after but to a lesser extent during work. Not only were the resting pulse rate and the rate during exercise in these cases increased (average increase in rate about 20 per cent), but the rate after exercise remained considerably elevated for several minutes instead of rapidly (1-2 minutes) returning to the pre-exercise level. The usual almost immediate slowing of the pulse rate after exercise noted in this group gives to the palpating finger an impression to which Allbutt must have been referring when, in describing the pulse during an attack of angina pectoris, he remarked, "Not uncommonly, to the sensitive finger, there is to be noted in one or more beats a deliberation, an impression of delay . . . it reminds one of the momentary self-collection of a horse before he leaps."²⁹ This sensation, as though the pulse were holding back, was noted only after exercise. This state was abolished by atropine.

We were able to observe the effect of six weeks of absolute bed rest in one of the patients (C.J.E.) who had considerable breathlessness preceding the cardiac pain and in whom we assumed early left ventricular failure to be present. This patient received no digitalis. During the first few days of his hospital stay where he was under Dr. J. H. Pratt's care he had a definite diuresis on a Karrell diet. This was interpreted as confirmatory evidence of presence of cardiac weakness. When he was seen some two weeks after the period of bed rest, his response to exercise was essentially unchanged, there being only a slight decrease in his pulmonary ventilation and obvious breathlessness during the exercise. His field of cardiac response, as measured by the amount of work necessary to produce pain, was practically unchanged. It is obviously unfair to conclude from this one case

that prolonged bed rest is of no value in this type of case. Perhaps the addition of digitalis might help. This same patient, before he was put to bed, reported marked improvement following the use of one of the adenosin preparations. Examination indicated that though there was a subjective sense of improvement the actual amount of work he could perform under fixed conditions before cardiac pain supervened was absolutely unchanged as was the response of his cardiovascular system to exercise. This case may be taken to indicate how unreliable are simple reports of improvement based on subjective observations.

Results With Quinidine Sulphate.—In both of the patients in whom extrasystoles were found to appear just before the onset of pain and to disappear shortly after the cessation of exercise, quinidine sulphate was employed in doses up to 0.4 gram, four times a day. On the assumption that the extrasystoles decreased the effective coronary flow during exercise and hence the supply of oxygen to the myocardium, we sought to abolish the extrasystoles and thereby increase the cardiac efficiency during exercise. This was possible with quinidine.

Thus one patient (L.K.) developed cardiac pain pedalling on a stationary bicycle under the same conditions with a fixed load and at a fixed speed in from four minutes twenty seconds to five minutes twenty seconds on six occasions within one week. Two days after the last of these observations when he was taking 0.5 gram of quinidine sulphate four times daily he was able to pedal for nine minutes and forty seconds (cf. Fig. 5), and when the pain did appear, it was definitely much milder than it was during the control period. During the control period this patient regularly developed auricular extrasystoles from forty to eighty-five seconds before the onset of his pain. The irregularity persisted from thirty to seventy seconds after the exercise. With quinidine, when he was able to do twice as much work before pain developed, there were no irregularities in the pulse before, during, and after the exercise. When the quinidine was discontinued for three days, the exercise tolerance dropped to five minutes and fifty seconds, and the irregularities reappeared in the manner described above. This patient has been taking 0.4 gram of quinidine sulphate three times a day regularly for five months. His exercise tolerance, last measured after four and one-half months of quinidine therapy, remained over ten minutes (exercise was stopped at ten minutes though there was no pain). He has worked as a janitor in a large school through a very severe winter with no great discomfort, although his duties have included shoveling snow, moving barrels of ashes weighing about 100 pounds, etc. Before quinidine therapy he had been unable to carry on his work even in the warmer weather of the fall.

Quinidine not only regulated the heart rate in this patient but also caused a greater and more rapid rise during exercise as well as a slower return to the pre-exercise level. The accelerating effect of quinidine differed from that of atropine in that the quinidine caused the rate to rise more quickly, though to no higher level. The sensation of deliberation or holding back of the pulse above referred to, which was noted in both patients of this group, was abolished both by the atropine and by the quinidine. This accelerating effect was apparently in no way responsible for the improvement in capacity to work, for when this effect wore off in a few days while the patient was still taking quinidine (heart rate 102 per minute during the

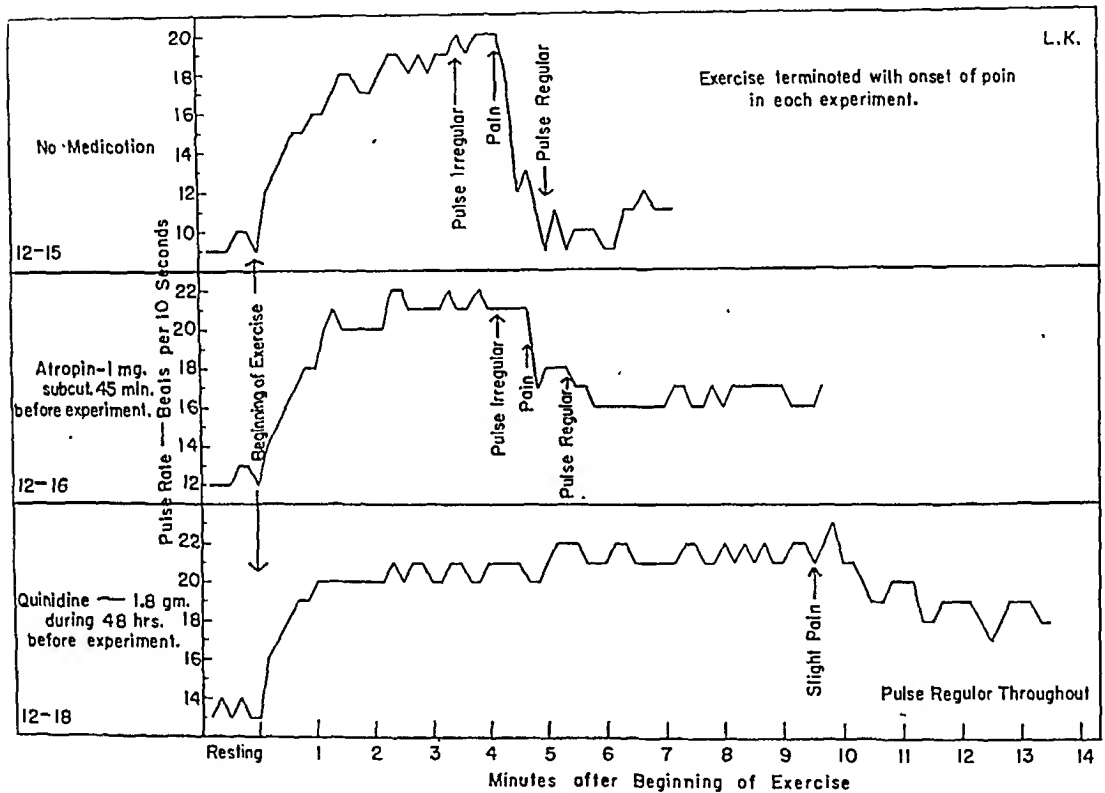


Fig. 5.

moderately severe work of the exercise tolerance test) the improvement continued. The irregularity, however, remained absent. This would indicate that it was simply the abolition of the irregularity which brought about the improvement.

A comparison of the effect of atropine and quinidine in the patient to whom we have just been referring is seen in Fig. 5 in which the quicker rise in pulse rate as well as the prolongation of the ability to perform the work is readily seen. This figure also illustrates the absence of any relationship between the level of the heart rate during exercise and the onset of pain in this patient.

The other patient who showed the same type of pulse rate response (cf. Fig. 3) developed pain on four occasions before quinidine after

pedalling 90 to 120 seconds; whereas after the irregularity had been abolished by the use of quinidine, he was able to pedal for four minutes, when he stopped because of fatigue and not because of pain. In this case, too, the pulse rate after quinidine rose more quickly to a higher level during exercise and remained at a high level for several minutes after the cessation of exercise.

In a third patient (E.L.) who had many extrasystoles before, during, and after exercise, quinidine sulphate was also given. In this case the irregularity was usually less marked during than before and after exercise. This patient was able to pedal on six occasions before the cardiac irregularity was abolished by quinidine sulphate for an average of four minutes and fifty seconds (variation three minutes, forty seconds to five minutes, twenty-five seconds). When the heart rate became regular, he was able to pedal from seven minutes, thirty seconds to eight minutes, when he stopped because of fatigue. In this case the quinidine did not have even an initial accelerating effect on the heart rate.

In two of the patients who exhibited only occasional single ectopic beats quinidine sulphate did not increase the capacity for work.

Because of the heart rate accelerating properties of quinidine the drug was given to two patients in whom there was a relatively slow pulse rate during exercise, in an attempt to learn whether the change in the pulse rate during exercise under these conditions might have some effect on the capacity for work. Since the accelerating effect of quinidine is only temporary, a prolonged effect on exercise tolerance was not anticipated. One patient (O.H.) showed no definite improvement; the other patient (L.N.) was able to double his capacity for work when his pulse rate rose more rapidly and to a greater level with quinidine. Unfortunately, only one observation could be made in this case after the control period because of the development of symptoms of quinidine intoxication. It is noteworthy that despite definite objective evidence of improvement this patient reported that he seemed no better. The fact that definitely more exertion was required to elicit the pain had not impressed itself on his mind. Even after the test when he was told he had done twice as much work as before, he seemed surprised; he simply knew that pain came on with exertion. This patient again illustrates how difficult is the evaluation of therapeutic effects in patients with angina pectoris, based on their own reaction.

On the other hand, we have one patient who kept a daily record for six weeks of the number of nitroglycerin (0.065 mg.) tablets he required for relief of pain in his daily work as a truck driver. He took the nitroglycerin only when the pain was severe. During this

period we made observations on his capacity for work under the conditions above described. A few months later when he spontaneously improved to the extent that he took no nitroglycerin for three weeks, his exercise tolerance as we measured it remained essentially unchanged. He insisted that his activities in his daily life were in no way changed and that he could definitely do more work without discomfort. The weather was essentially unchanged. This leads us to suspect that

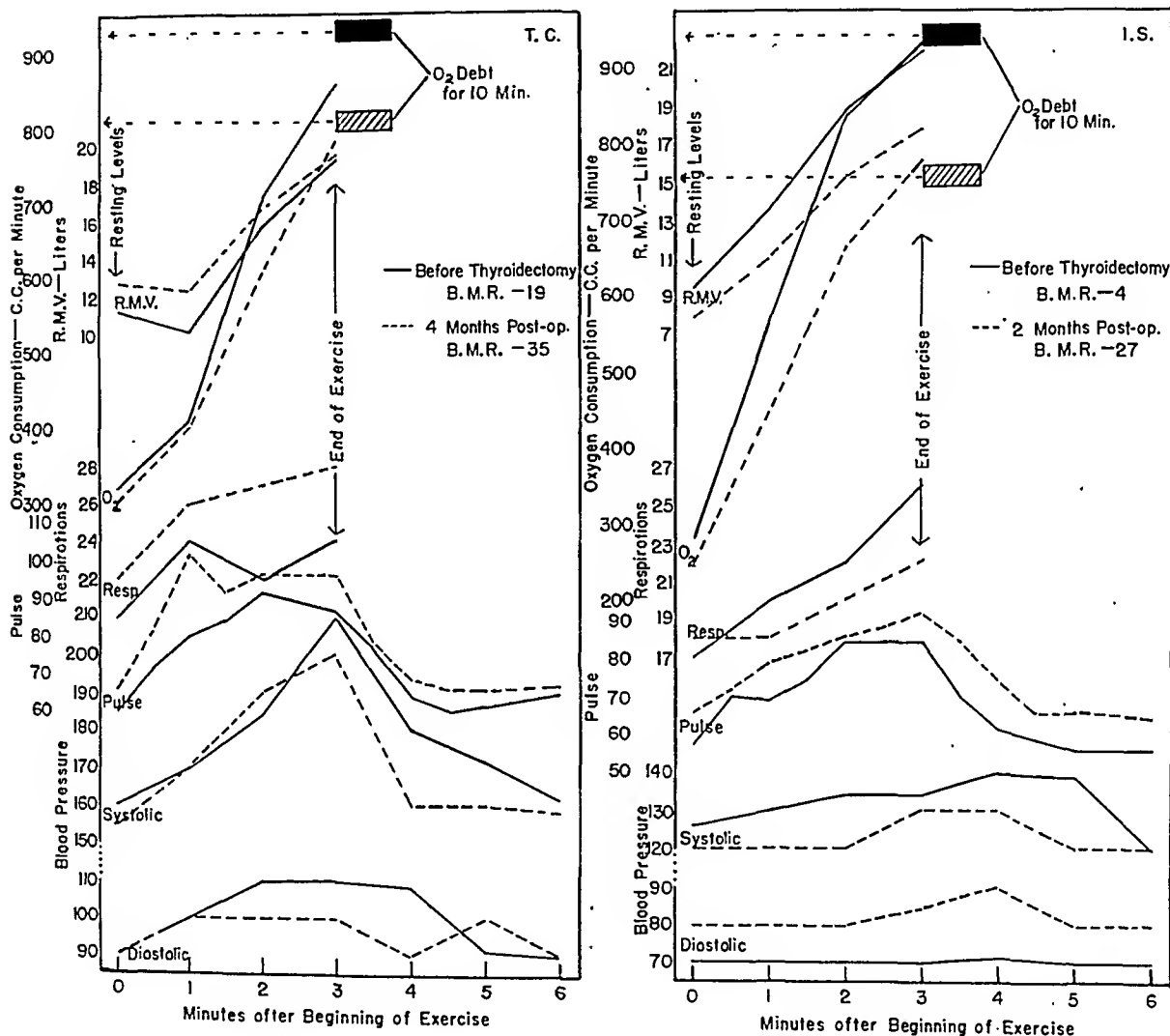


Fig. 6.

there is not necessarily a direct relationship between true clinical improvement in angina pectoris and changes in standard exercise tolerance tests.

Effect of Total Ablation of Thyroid.—Four patients with angina pectoris were studied before and after total thyroidectomy. The operations were performed by Drs. D. Berlin and E. C. Cutler of the Beth Israel Hospital and Peter Bent Brigham Hospital, respectively. In two of the patients there was considerable relief following the op-

eration; in two the relief was only slight. Examinations were made postoperatively when clinical signs of myxedema were just appearing, and, except in one case, before thyroid substance was administered. Fig. 6 represents the results in one of the two patients (T.C.) who showed definite improvement both subjectively and objectively (stair-climbing tests under Dr. Riseman's supervision at the Beth Israel Hospital) and in one of the two patients who showed only slight improvement. In both cases there was a slight decrease in the level of oxygen consumption during exercise and perhaps a slight decrease in oxygen debt (differences here recorded for oxygen debt are within the range of our experimental error). There was no significant difference in either patient in respiratory rates or pulmonary ventilation before and after thyroidectomy; neither was there any essential difference in the two patients in the response of the pulse rate to exercise, the rate in both cases reaching a higher level after the operation than before. This change in pulse rate was perhaps more striking in the patient who showed considerable improvement than in the patient in whom improvement was only slight. However, in general it can be said that there was no striking difference in the postoperative response in these two patients which might account for the difference in improvement. Perhaps the reason for this difference lies in the presence or absence of varying degrees of fixed pathological changes.

Effect of Lowering Basal Metabolism by Dietary Restriction.—Considerable interest has been attached of late to the importance of the basal metabolic rate in patients with heart disease. Total thyroidectomy has been performed in an attempt to reduce the strain on the heart by lessening the need of tissues for oxygen.^{16, 22, 30}

Almost twenty years ago Benedict, Miles, Roth, and Smith,³¹ in an important and comprehensive research demonstrated that a very effective and simple method of reducing the level of tissue metabolism was by the use of moderate dietary restriction over a period of several weeks. In a group of healthy young college students they were able to produce a lowering in the average basal metabolic rate of about 20 per cent by a moderate restriction in diet which led to an average loss of about 10 per cent in body weight in two months. There was thus a decrease of approximately 30 per cent in oxygen consumption. This figure was further substantiated by the fact that in the next two months the body weights remained practically unchanged with a caloric intake which was lower by approximately one-third than it was at the beginning of the experiment. It is significant that not only the level of oxygen consumption at rest but the level at work as well was lowered in the same general ratio. This change took place

with no real impairment in health. The authors made the statement, "The beneficial effects in many pathological cases of lowering the metabolism perceptibly will, it is confidently believed, be demonstrated in the near future."

It seemed to us that the pathological cases in which such a state would be extremely desirable are those with cardiac weakness. Observations are being made at present on the effects in patients with chronic myocardial disease of lowering the body metabolism by dietary restriction.³²

It seemed also that by the use of dietary restriction we could determine whether it is the lowering of the basal metabolic rate which is responsible for the improvement which has recently been observed

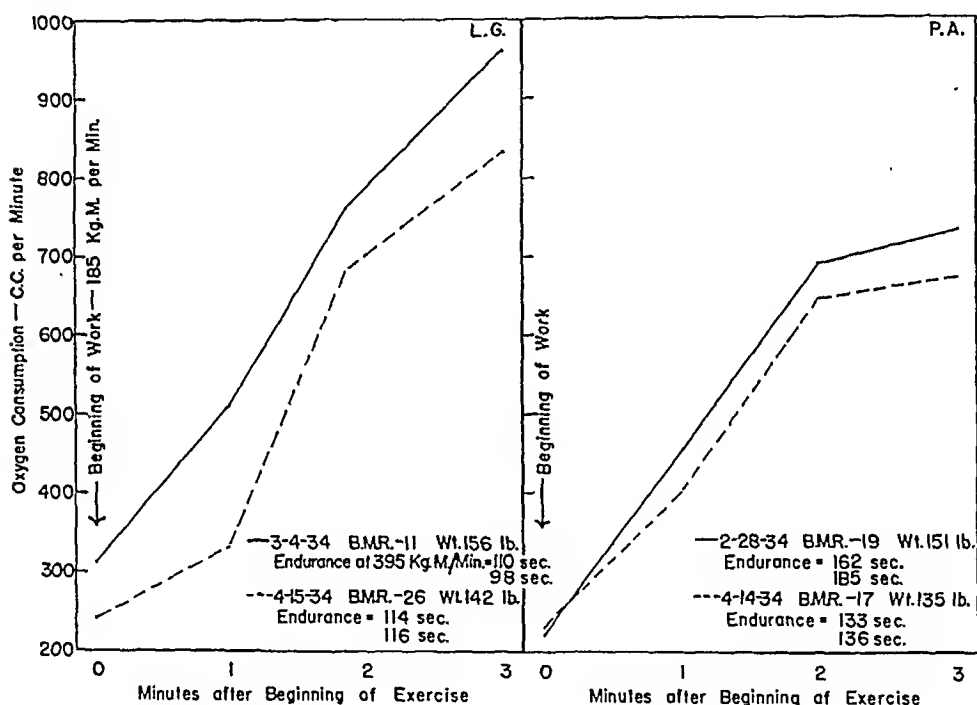


Fig. 7.

in patients with angina pectoris who have had total thyroidectomies, or some other as yet unknown change associated with the operation itself or the hypothyroid state. With this in mind, we placed two patients with angina pectoris, who apparently responded normally to the exercise tests above described. In one case (P.A.) the initial basal metabolic rate was minus 19 per cent. There was no drop in the basal metabolic rate in this patient. In the other patient (L.G.) the initial basal metabolic rate was minus 11 per cent. In this case a drop in the basal metabolic rate of 15 per cent with a loss in body weight of about 10 per cent was followed by no improvement in capacity for work. There was associated with the lowered basal metabolic rate a lower level of oxygen consumption during work, a slower pulse rate, slightly lower blood pressure at rest (no essential change

during work), and a slightly lower resting circulation time. Despite the drop in oxygen consumption and other apparently more favorable conditions for the cardiovascular mechanism, the angina pectoris remained unimproved as measured by exercise tolerance tests. The changes in oxygen consumption during work in the two patients are illustrated in Fig. 7. An adequate preliminary period of training eliminated a training effect as a source of error in interpretation.

This would indicate that some factor other than the hypometabolism is responsible for the prolonged improvement seen in angina pectoris following thyroidectomy. One of these factors may presumably be the general diminution in sensitiveness to all forms of sensation. Patients with myxedema seem slower to appreciate ordinary painful or otherwise uncomfortable stimuli, nor do they respond so acutely. Perhaps that is the reason why in two of our patients who had total thyroidectomies the remark was frequently made that even when the pain did develop it was not so severe.

SUMMARY AND CONCLUSIONS

1. Seventeen patients with angina pectoris and six normal controls in the same age group were studied in the following manner: The subjects pedalled on a stationary bicycle at a fixed load and speed for three minutes. The blood pressure, pulse rate, respiratory rate, pulmonary ventilation and oxygen consumption were measured before, during, and after (oxygen debt) the exercise. The oxygen consumption was measured during each minute of the exercise.

2. There were four general types of response in the patients with angina pectoris, the most significant disturbance in these groups being: (I) failure of the heart rate to increase normally during exercise; (II) the development of cardiac irregularity (extrasystoles) shortly before the onset of pain and its disappearance shortly after the cessation of exercise; (III) a thin, thready, rapid, barely palpable pulse during exercise associated with a failure of the pulse pressure to increase normally with a return to normal shortly after the cessation of exercise; (IV) primary respiratory distress with rapid pulse rate characteristic of cardiac weakness. In each group the disturbances might be interpreted as favoring the development of myocardial anoxemia.

3. In two of the patients the response to exercise was considered normal.

4. The variety of types of response to exercise was taken to indicate that angina pectoris is merely a symptom which may be a manifestation in different people of widely different disturbances.

5. In Group I the administration of atropine permitted the heart rate to rise to a higher level during exercise but did not increase the ca-

capacity for work without pain. In one patient in Group III absolute bed rest for six weeks was followed by no demonstrable objective signs of improvement.

6. In Group II the abolition of the cardiac irregularity by the use of quinidine sulphate resulted in a striking increase in capacity for work without pain.

7. Four patients were observed before and after thyroidectomy. Clinical improvement did not parallel changes in response to work, these changes being a slightly greater increase in pulse rate during exercise where it had been abnormally low before the operation and a lower level of oxygen consumption during exercise as well as at rest.

8. Lowering of the level of oxygen consumption at rest and during exercise by means of a prolonged restricted diet did not increase the capacity for work without pain in one patient.

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THE REESTABLISHMENT OF CARDIAC CIRCULATION DURING PROGRESSIVE CORONARY OCCLUSION*

AN EXPERIMENTAL STUDY ON DOGS

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THERE are numerous reports of hearts having continued their functions while the coronary vessels were more or less occluded.¹⁻⁶ Four main explanations for this phenomenon are found in the literature. (Fig. 1.) First, there is the so-called "thebesian backflow" theory. Recent investigators have amplified, by excellent anatomical studies, previous records concerning vessels that run in the myocardium between the arteries and veins of the heart and the heart cavities.^{2, 6-8} It has been suggested that blood might enter the heart wall from the heart cavities along these channels spoken of, respectively, as vessels of Vieussens or of Thebesius after their original discoverers.^{6, 7, 10-13} Full proof that these vessels may perform this function is lacking; indeed, the explanation requires further physiological support.¹⁴ Such a backflow into the myocardium would be quite extraordinary during systole when the intramural pressure is at least 50 mm. Hg higher than the intraventricular pressure. During diastole, pressures are more nearly equal, but whether the intracardiac pressure is ever great enough in diastole to force blood into the heart walls is still to be proved. That some ebb and flow takes place seems possible from certain data.^{1, 6, 10-13} Second, there is the suggestion that a compensatory blood flow by way of intercoronary vessels, epicardial vessels, including the rami telae adiposae, and their various thoracic anastomoses through the aortic vasa vasorum, may feed the myocardium.⁵ Epicardial vessels have been shown to bridge widely occluded gaps in the coronary circulation, and there is no doubt that ramifying intercoronary vessels play a major rôle in maintaining many hearts with partial occlusion.³ Very meager evidence, however, has been presented that these vessels might receive sufficient blood from aortic vasa vasorum to sustain the myocardium when the coronaries were completely or almost totally occluded. Third, it has been suggested that venous backflow from the right auricle via the coronary sinus might suffice to nourish the heart.^{2, 10} Such a sinus backflow could be for only a very brief period in each cardiac cycle because the auricle's small positive pressure barely precedes the abrupt and extensive rise

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in coronary sinus and venous pressure which accompanies ventricular systole. As the veins were tied off in the first stage of our experiments, a test of this theory here was immediately ruled out. Fourth, it has been shown by experiment that adhesions between the heart and the thoracic viscera may carry numerous vessels to the heart wall. This method of supply is uncommon in human material, and in experimental studies such vessels played a minor rôle in the heart's blood supply.¹⁵

It is certain from the above data that certain hearts do receive sufficient nutrition for their functions in some way while their main source of supply is diminished. Experiments with isolated or partially isolated hearts tend to confirm this finding, the majority of workers

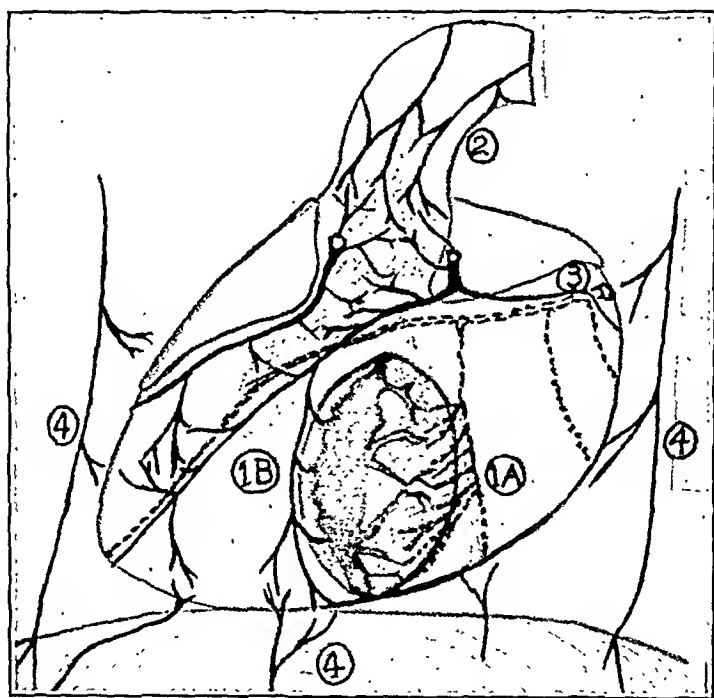


Fig. 1.—Four suggested sources of blood supply to myocardium when the coronaries are closed.

1. Backflow from heart cavities into heart wall through (A) vessels of Thebesius, (B), vessels of Vieussens.

2. Coronary vessel anastomoses through vasa vasorum of great vessels with the thoracic vessels.

3. Backflow from right auricle along coronary sinus into heart wall.

4. Vascularized adhesions between the thoracic wall, thoracic viscera and diaphragm, and the pericardium and heart.

favoring the "thebesian backflow" theory, a few adding to this the "coronary sinus backflow" theory, as the *modus operandi*. However, many isolated mammalian hearts may function well for some time on little nutrition, and perfusion experiments rarely parallel conditions in human material. Stella's careful experiment indicated that no backflow from the heart cavities to the cardiac vessels actually occurred in the normal heart.¹⁴ Whether any change occurs in abnormal hearts favoring a backflow from the heart cavities into the heart wall,

awaits further proof. It, therefore, seemed reasonable to put the matter of cardiac nutrition during coronary obstruction to actual test in the living animal by producing gradual coronary occlusion and noting in what manner myocardial circulation was reestablished.

METHOD

The experimental method was as follows. The coronary sinus and the main veins of the heart were tied in from one to three stages before arterial ligation was commenced to encourage dilatation of the thebesian vessels and of the coronary vessels generally.^{16, 17} The coronary arteries were then tied in several stages, the average animal having all main veins and arteries ligated at the end of six operations. The hearts were closely watched at each stage for evidence of developing cardiac, pericardial, aortic, and thoracic anastomoses; and for any increase in the size or vascularity of the epicardial and periaortic fat pads or the pericardial fat. Finally, in the surviving dogs, the very vascular pericardial adhesions formed during these procedures were stripped from the hearts to judge what part they took in nourishing the myocardium and to see whether thebesian-like vessels, the only likely remaining source of blood supply to the heart, could support cardiac function.

A typical protocol is as follows: Dog B-98-33. Young, female police dog, 15 kg. wt. Intertracheal ether and Erlanger respirator were used throughout. Except as noted in the last procedure, the chest was always opened by intercostal incision, closure being done in layers.

Procedure I: February 20, 1933. Left chest was opened. Heart showed normal vascular distribution. Coronary sinus was tied between posterior central vein and right auricle. There was immediate bulging of sinus and all veins of left heart. Bluing of left heart wall commenced and small vessels previously invisible appeared. In five minutes arterial dilatation was moderate and petechial-like spottings were seen over the main vessels about which white fluid had gathered under the epicardium which was raised. During this time the heart rate slowed and contractility decreased. Chest was closed. Postoperative condition good. *Procedure II:* March 8, 1933. Right chest was opened. Veins of right heart were normal, anastomoses between great cardiac vein and middle cardiac vein were enlarged. Veins were tied off, heart was unaffected, chest was closed, condition was good. *Procedure III:* April 26, 1933. Left chest was reopened. Pericardium was laden with avascular fat, many vascular adhesions between vessels of pericardium and epicardial vessels of left heart, all of which were increased in number and size, especially at the apex. Great cardiac vein and anterior descending ramus of left coronary were tied just under the tip of the left auricular appendix. No change in color of heart or rate of beat. Chest was closed. Condition was good. *Procedure IV:* May 19, 1933. Right chest was reopened. Many vascular adhesions to right margin heart and about apex where the whorl of vessels was present. All branches (4) of right coronary were tied just at auriculoventricular groove. Heart slowed and contractility was lessened; there was bluing of the posterior apical region of the heart. Chest was closed. Immediate recovery was good, but later there was moderate edema of the legs lasting two weeks, then complete recovery. *Procedure V:* July 12, 1933. Left chest was reopened. Fat of mediastinal septum and pericardium markedly increased and very vascular; vascularized bands from chest wall and diaphragm to pericardium, through this to heart wall. Left marginal branches of left coronary were tied, the left coronary itself was tied without production of cyanosis or change in rhythm. Right coronary was tied. Condition was good. *Procedure VI:* August 18, 1933. Sternum was split and profuse vascular adhesions were seen from the chest wall and

diaphragm and lungs to pericardial vessels which in turn joined myocardial vessels by virtue of the adherent pericardium. Pericardium was stripped from myocardium, numerous vascular adhesions being cut and tied, leaving many patches of cyanosis. Chest was closed and dog remained well for a time with slight edema of legs. This gradually increased and after one remission of two weeks' duration the dog died in October of cardiac failure. This was the only animal to survive the last procedure of the experiment for more than a few hours.

OBSERVATIONS

Our observations will be grouped briefly under the various operative stages of the experiment. The venous ligatures were well tolerated by all animals. The left heart of some animals, when the coro-



FIG. 2.—A slide from a serial section study of a heart after coronary sinus, coronary veins and coronary arteries had been tied. Arrows follow two large vessels from heart cavity through left heart wall to two epicardial vessels, one an artery, one a vein. These vessels were commonly seen.

nary sinus was tied, showed more cyanosis, more temporary venous engorgement, and a greater amount of coronary artery dilatation than did others. This variation depended on how well the thebesian vessels responded to the extra load on their ordinary function of draining the heart wall of blood not carried off by the various cardiac veins. The sinus ordinarily drains off two-thirds of the heart's blood, chiefly the left heart's. When the sinus is closed, this blood is forced into the heart cavities through thebesian channels or through the *venae cordis minimae*. It cannot be said definitely to what extent accessory vessels were enlarged by this procedure; but serial sections from the

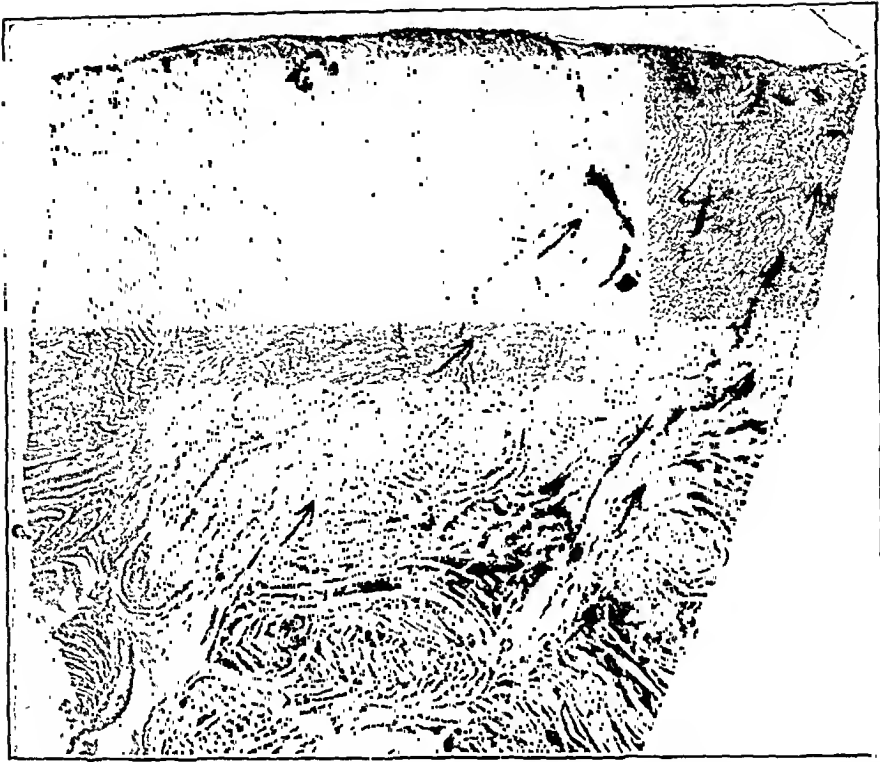


Fig. 3.—A slide from a serial section study of a heart after coronary sinus, veins, and coronary arteries had been tied. The vessels indicated by arrows penetrate the full thickness of the left heart wall, are quite dilated, and make wide anastomoses during their course.

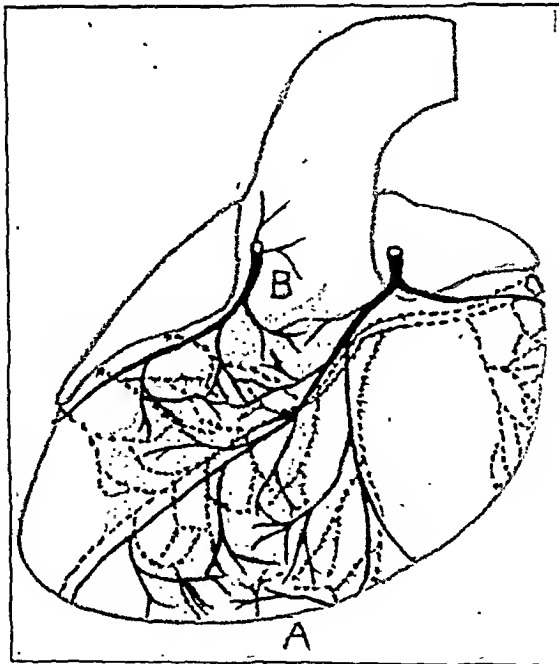


Fig. 4.—Typical areas of vascular, especially venous, enlargement and proliferation following ligation of the coronary sinus. (A) Apical region where veins of great cardiac vein anastomose with veins of the posterior longitudinal sulcus. (B) Region of conus arteriosus where branches of the great cardiac vein anastomose with right heart veins and veins of the great vessels.

hearts showed large vessels, connecting the heart cavities with the epicardial vessels, widely open at the end of the experiments (Figs. 2 and 3). By the time the main veins and any large tributaries had been tied, scanty adhesions amounting to avascular fibrinous deposits had formed between the heart and the pericardium but were easily separated. Frequently a whorl of enlarged veins was present at the apex of the heart and in other anastomotic regions such as the conus arteriosus (Fig. 4).

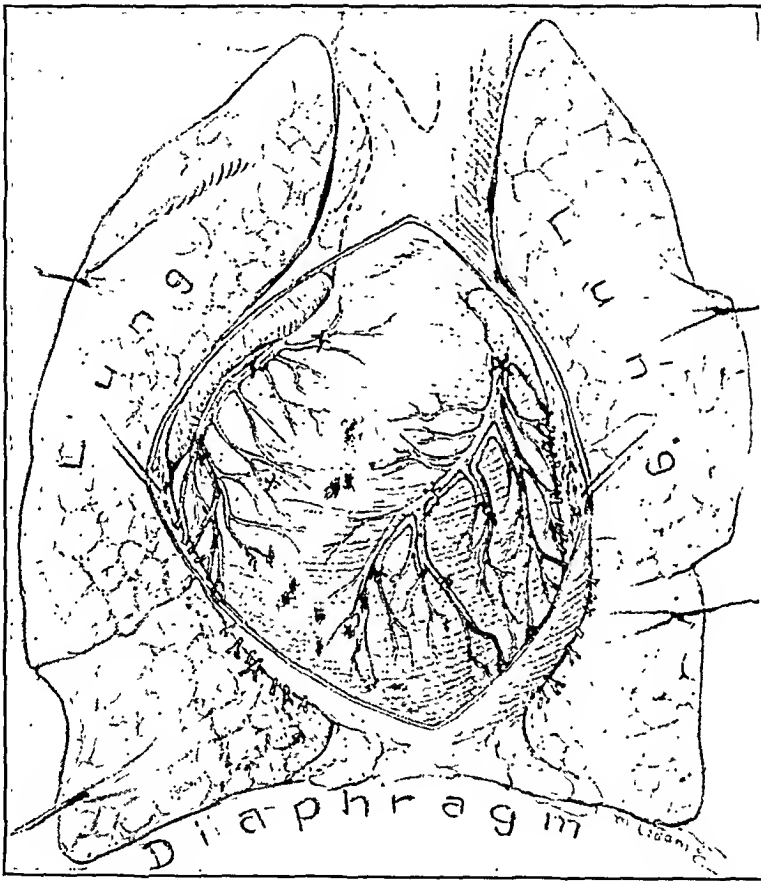


Fig. 5.—Vascular adhesions nourishing the heart wall after all vessels ligated.

Ligature of the smaller branches of the right and left main coronary stems, then the main stems, a short way from their origins, was carried out without mishap even though at the latter stage quite firm and vascular adhesions were often present which stripped from the heart with difficulty. The majority of the hearts showed a whorl of arteries and veins at the apex. This was best developed in hearts which had shown unusual cyanosis and vascular dilatation of the left heart following venous ligation. A similar change was found over the conus arteriosus. Both areas are sites where coronary anastomoses develop readily (Fig. 4). A few of the hearts showed an increase in epicardial

fat, especially in the anastomatic areas just mentioned, where venous congestion was or had been marked; but the fat was not vascularized to any extent though found in areas more vascular than usual. No evidence of increased anastomoses between the aortic vasa vasorum and the epicardial vessels was found.

The final coronary ligation closed the main trunks at their origins, any accessory vessels found being also tied. The dogs all survived this final procedure for at least some hours; the majority, however, died in twenty-four to forty-eight hours. Three suffered little or no ill effect. All the animals showed a great increase in vascularity and density of the pericardial adhesions, the vessels of which formed well-defined anastomoses between various thoracic vessels and the heart wall, especially marked along the course of the phrenic and internal

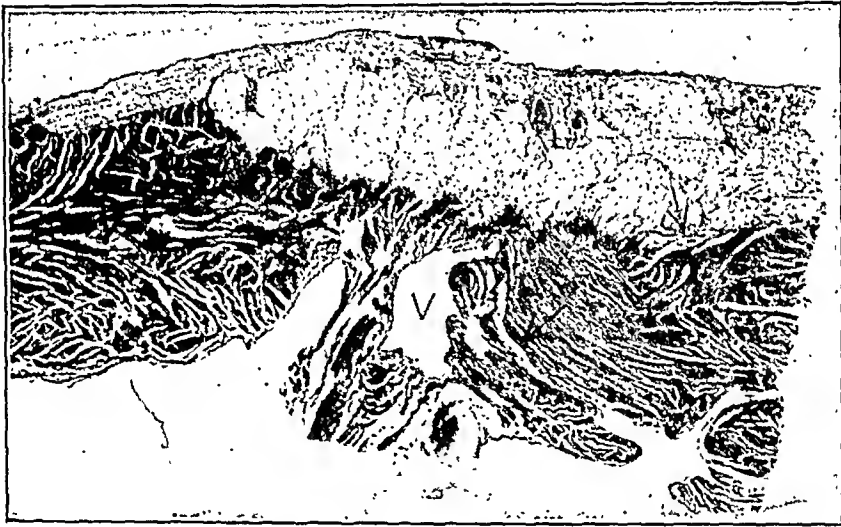


Fig. 6.—Section from heart wall after coronary artery and vein occlusion. Large channels run into the inner myocardium from the interstices between the trabeculae carneae. Although the inner heart wall is well nourished, these channels approximate an area of muscular degeneration and fatty infiltration occupying the outer half of the heart wall which they apparently could not nourish. Other sections showed degeneration of outer half of the heart wall with intact inner half of wall and no demonstrable thebesian-like vessels. The presence or absence of thebesian-like vessels seemed to have little to do with the state of myocardial nutrition.

mammary vessels (Fig. 5). These vascular adhesions were, of course, partially severed in tying the coronaries. Their separation and ligation produced definite areas of cyanosis of the heart wall. The actual ligation of the coronaries produced very little or no change in the appearance of the heart wall. As a rule, it was the animal whose heart appeared to be so largely nourished by the thoracic adhesions that survived only a short time. In these fresh infarctions were found at autopsy at points indicating that the vascular supply from other sources than the pericardial adhesions had been insufficient for cardiac vitality. It was felt that, though some trauma was done the hearts, it had not been sufficient by itself to cause the postoperative deaths.

There was no further increase in epicardial fat or epicardial anastomosing vessels, and no enlargement of aortic vasa vasorum was seen.

The three animals surviving complete coronary ligation were opened later, and the pericardial adhesions were completely separated. A definite increase in pericardial fat was found, largely avascular. There was only a slight increase in the epicardial fat over the increase seen following the first arterial closures. Proliferative vascular adhesions were present arising from many sources, chiefly from the phrenic vessels, the internal mammary vessels and from pulmonary vessels which had appeared at the lung borders to grow into the pleuropericardial adhesions (Fig. 5). The separation and ligation of these vascular adhesions left areas of cyanotic heart muscle obviously infarcted. Only one animal survived the operation; the others died in twelve to twenty-four hours from typical cardiac failure. Widespread recent infarction was found at autopsy; and evidences of previous sclerosing infarctions patently from the former ligations. The one survivor developed edema of the legs with hydrothorax and a permanent auricular fibrillation. After several weeks the animal recovered for a time but edema again occurred and the animal died with all the signs of cardiac insufficiency. The heart was found to have redeveloped vascular pericardial adhesions, but areas of recent infarction were present throughout the heart muscle. The cardiac failure was not complicated by an element of adhesive pericarditis.

Microscopic sections of the hearts showed varying degrees and stages of degeneration and fibrosis of the outer heart wall. The endocardial half was nearly always well preserved, but this could not be shown to be particularly associated with the occurrence of dilated vessels of the thebesian type (Fig. 6).

SUMMARY

There were two plausible routes by which these hearts could have been nourished, by the vascularized pericardial adhesions or by the vessels of Vieussens or Thebesius. The above observations indicate that little or no nutritive function developed in those channels known as the vessels of Vieussens or Thebesius, which penetrate the myocardium from the heart cavities. Myocardial nutrition distinctly depended on the vessels contained in the pericardial adhesions. The microscopic findings, indicating little disturbance in the nutrition of the endocardial part of the myocardium, do not justify the conclusion that this part of the heart was fed by thebesian-like vessels. Inter-coronary branches might have carried out this function.

There was no evidence of an anastomosis developing between the epicardial or intercoronary vessels and the thoracic vessels via the

aortic vasa vasorum to nourish these hearts. It is possible that in this experimental study the prolific vascular adhesions formed as an unavoidable sequel to the method employed superseded the development of other sources of cardiac nutrition.

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THE ELECTROCARDIOGRAM IN BROWN ATROPHY OF THE HEART*†

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ELECTROCARDIOGRAPHIC records exist in a wide variety of cardiac lesions. However, changes of the electrocardiogram in brown atrophy of the heart have apparently not been described. As a matter of fact, the literature contains no statement as to electrocardiographic records of patients who, at subsequent autopsy, showed brown atrophy of the heart. During the past year we have encountered three instances of brown atrophy of the heart, in each of which the electrocardiogram presented significant changes. In this report a short summary of the clinical, autopsy and electrocardiographic findings is given, and the significance of the electrocardiographic changes is discussed.

CASE REPORTS

CASE 1.—A white male, aged sixty years, was admitted to the hospital because of symptoms referable to peptic ulcers or gastric carcinoma. There were no significant cardiac findings elicited clinically. The autopsy revealed a primary carcinoma of the stomach. The heart was a small organ, weighing 200 grams (the body was emaciated, weighing about 92 pounds). The heart was diminished in size, about equally in all dimensions. The subepicardial fat tissue was transformed into a gelatinous material. The left ventricular myocardium measured about 7 mm. in thickness, the right 2 mm. There was some coronary arteriosclerosis. The myocardium was of a reddish brown color.

The patient died as the result of a bilateral confluent bronchopneumonia with abscess formation.

Electrocardiograms were taken as a routine procedure (cf. Fig. 1). There is a sinus rhythm. The QRS complex is small in Lead I, and inverted in Leads II and III, an appearance present in this patient for at least three years before death. Lead IV shows a small QRS, directed mainly downward.

CASE 2.—A sixty-four-year-old male was admitted to the hospital because of jaundice and pains in the abdomen radiating toward the back. The clinical diagnosis was primary carcinoma of the pancreas. There were no clinical findings significant of myocardial changes. The autopsy revealed a primary carcinoma of the head of the pancreas, with obstruction of the common bile duct and metastasis to the liver. The heart weighed 275 grams (the body was well nourished, weighing about 160 pounds). The heart was reduced in size about equally in all diameters. The subepicardial fat tissue was scanty. The left ventricular myocardium measured about

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†Aided by the Frederick K. Babson Fund for Diseases of the Heart and Circulation.

12 mm. in thickness, that of the right 2 mm. There were moderate arteriosclerosis of the coronary vessels and slight myocardial fibrosis. The heart muscle was deep brown.

The patient died as the result of a pulmonary embolus arising from a thrombus in the common iliac vein.

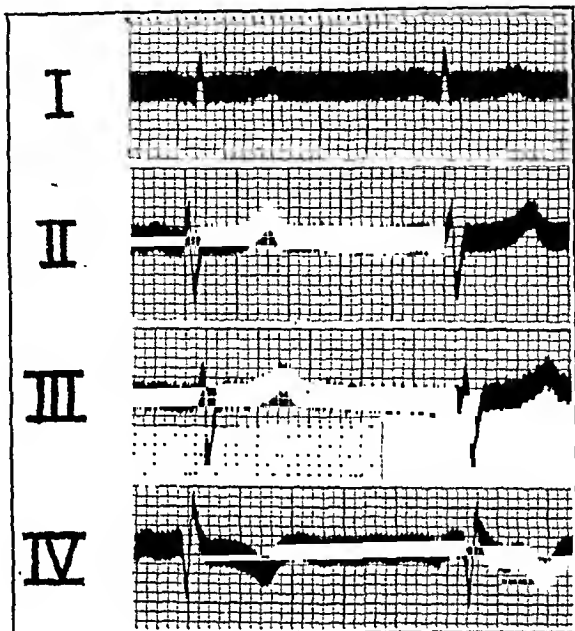


Fig. 1.

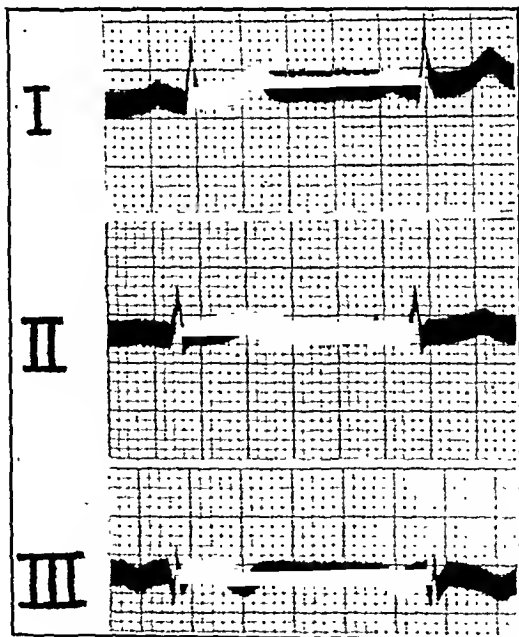


Fig. 2.

The electrocardiogram (Fig. 2) shows a sinus rhythm and occasional auricular extrasystoles, small amplitude of QRS in Leads II and III, and a relatively small amplitude in Lead I. The T-wave is inverted in Lead III. The record shows a slight left axis shift, but the changes are all within normal limits.

CASE 3.—A forty-five-year-old male was admitted to the hospital because of a diffuse enlargement of the lymph nodes and evidence of portal obstruction. There were no clinical symptoms referable to myocardial changes. At autopsy there was a lymphosarcoma involving the mesenteric, retroperitoneal, inguinal, tracheobronchial, and cervical lymph nodes, the spleen, liver and kidneys. The heart was distinctly atrophic, weighing only 250 grams (the body weighed about 180 pounds). The heart seemed uniformly reduced in size. The subepicardial fat tissue was transformed into a gelatinous material. The myocardium was dull, deep brown, and soft. The right ventricular myocardium measured 1 mm. in thickness, the left 8 mm. The coronary arteries were patent throughout. There was only a slight coronary arteriosclerosis.

The patient died of a bilateral confluent bronchopneumonia.

The electrocardiogram (Fig. 3) shows a sinus rhythm, QRS inverted in Lead III, and QRS relatively small in Leads II and III. The T-wave is small in Lead III. There is a left axis shift but the record is within normal limits.

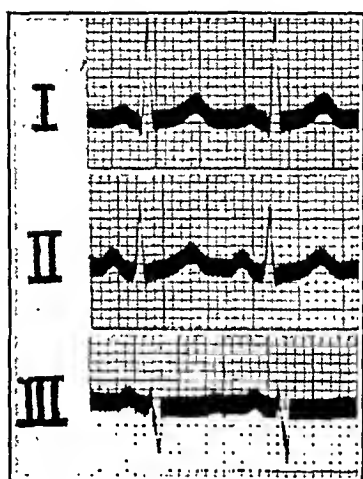


Fig 3.

It is interesting that in each case there was left axis shift, in Case 2 slight, in Case 3 moderate, and in Case 1 marked. A record such as that obtained in Case 1 is customarily considered *prima facie* evidence of a left ventricular preponderance and presupposes a hypertrophied heart. It was, therefore, a surprise to find the heart, at autopsy, actually smaller than normal. It is true that in each of these hearts there were other cardiac lesions present, but none of these can explain the axis shift. There was no evidence of any obviously altered position of the heart to account for the axis shift. Perhaps the axis shift came about because the reduction in size was less in the left than in the right ventricle, but the evidence obtained post mortem is not clear-cut on this point.

It follows from this observation that left axis deviation, even of advanced degree, is not in itself evidence of hypertrophy, but it may occur not only in a normal sized heart but also in an atrophied one.

SUMMARY

The electrocardiograms in three instances of brown atrophy of the heart are described. Emphasis is placed on the occurrence of left axis deviation in each of these records. Left axis deviation, even of advanced degree, cannot therefore be taken by itself as evidence of cardiac hypertrophy since it can occur in an atrophied heart.

EFFECT OF DIGITALIS ON THE APPEARANCE OF LEAD IV*†

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IT HAS been shown that in recent coronary occlusion characteristic diagnostic changes are to be found in Lead IV of the electrocardiogram.¹ In view of the rapid changes commonly occurring in the ordinary leads following the administration of large quantities of digitalis, it appears not unlikely that the contour of Lead IV also may be altered by digitalis. In fact, on several occasions the interpretation of changes in Lead IV has been complicated by the fact that the patients had been receiving digitalis. We therefore decided to study the effect of digitalis on Lead IV.

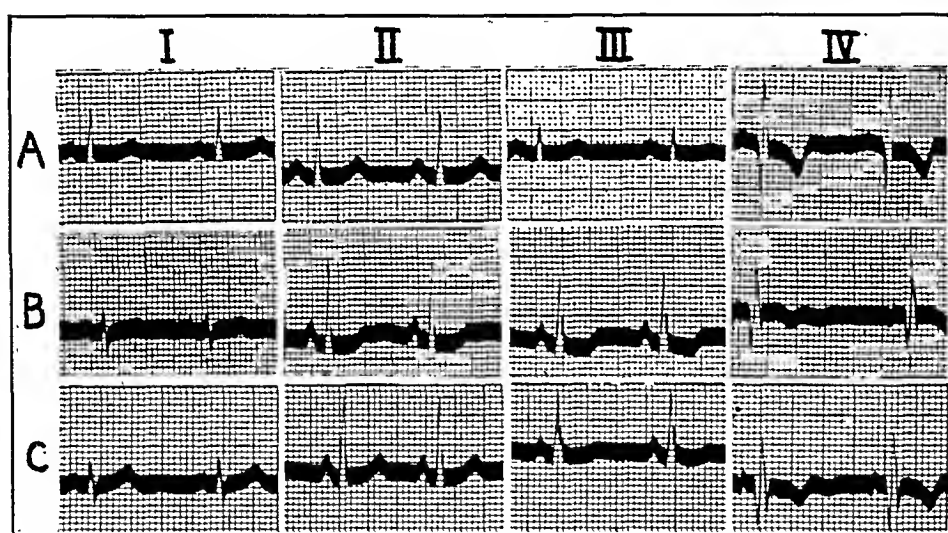


Fig. 1.—Four lead electrocardiograms obtained in Subject 1 (Table I): *A*, control; *B*, segments taken one day after digitalis was stopped; *C*, segments taken three days after digitalis was stopped (note the persistence of some of the changes in segment *C*, also the right axis shift).

The present report deals with such a study on 13 subjects, 7 being normal individuals in whom digitalis intoxication was experimentally induced and the other 6 being cardiac patients with various types of lesions, in whom digitalization was demonstrable clinically and in the standard three leads of the electrocardiogram. The procedure in the normal individuals was to digitalize them up to the point of toxicity and to compare the appearance of the four-lead electrocardiograms taken at this time with the contour before digitalis was started. Additional records were also taken for comparison at intervals after

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†Aided by the Frederick K. Babson Fund for Diseases of the Heart and Circulation.

stopping the digitalis. Four-lead records were taken in the cardiac patients at the height of the digitalization and at various intervals after digitalis had been stopped.

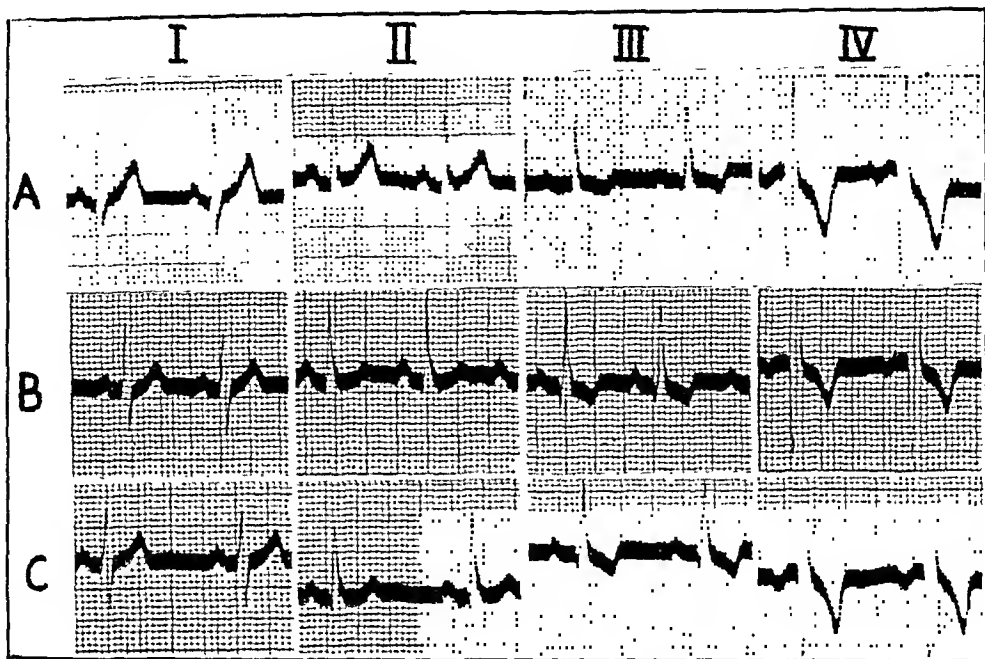


Fig. 2.—Four lead electrocardiograms obtained in Subject 5 (Table I): *A*, control; *B*, segments taken one day before digitalis was stopped; *C*, segments taken three days after digitalis was stopped.

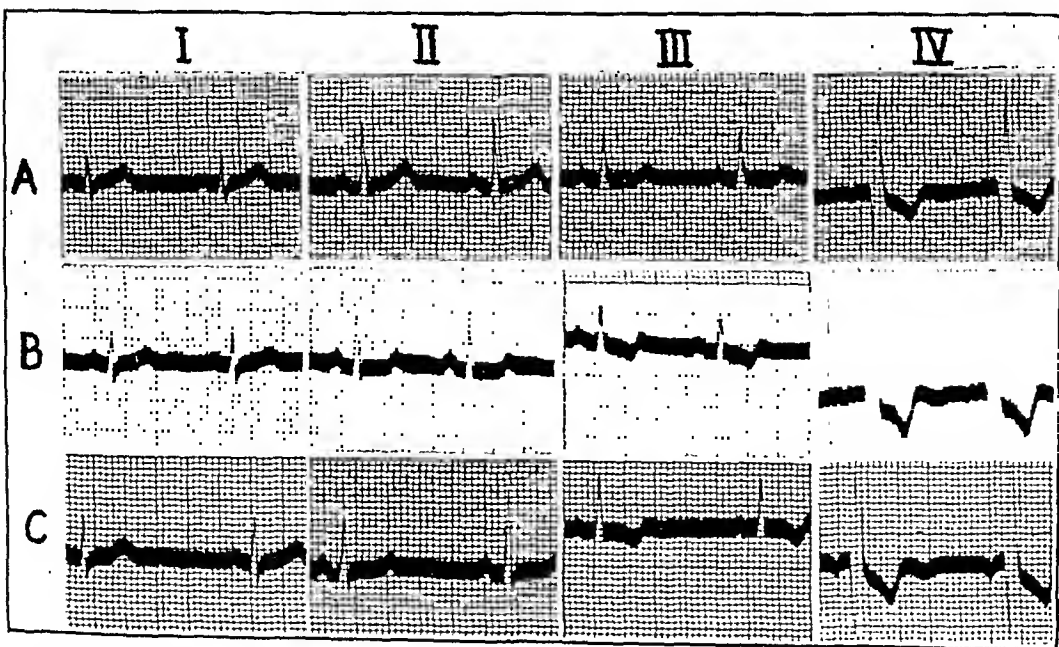


Fig. 3.—Four lead electrocardiograms obtained in Subject 7 (Table I): *A*, control; *B*, segments taken one day after digitalis was stopped; *C*, segments taken eight days after digitalis was stopped.

The results obtained are briefly summarized as far as Lead IV is concerned in Table I and illustrative curves shown in Figs. 1 to 4. The chief changes seen in Lead IV were in the S-T segment and T-

wave, and these were reversible on discontinuing the digitalis. The changes in the S-T segment in Lead IV were variable. It became positive in 5 instances (cf. Figs. 1 and 4), depressed in 4 (cf. Fig. 3), and unchanged in 3 (cf. Fig. 2). In one instance the S-T changed from a slightly negative to the isoelectric level. The negative T-wave in Lead IV became smaller in every instance (cf. Figs. 1, 2, and 3),

TABLE I
CHANGES IN LEAD IV PRODUCED BY DIGITALIS

SUBJECT NO.	DIGITALIS		CHANGES IN LEAD IV FOLLOWING DIGITALIS		REMARKS
	AMOUNT TAKEN GRAINS*	TAKEN OVER DAYS	S-T SEGMENT	T COMPLEX	
1	24	3	Became positive	Became smaller	Normal
2	27	3	Became negative	Became smaller	Normal
3	24	4	No change	Became smaller	Normal
4	39	9	Became isoelectric	Became smaller	Normal
5	45	5	No change	Became smaller	Normal
6	30	5	No change	Became smaller	Normal (inactive rheumatic heart disease)
7	36	3	Became negative	Became smaller	Normal
8	42	14	Became positive	Disappeared	Aged 40. Rheumatic heart disease, auricular fibrillation.
9	94	21	Became positive	Disappeared	Aged 44. Rheumatic heart disease, congestive heart failure, auricular fibrillation, pulsus bigeminus, complete A-V block.
10	54	9	Became negative	Became positive	Aged 55. Diabetes mellitus, hypertension, congestive heart failure, sinus rhythm.
11	26	9	Became negative	Became smaller	Aged 52. Diabetes mellitus, coronary sclerosis, sinus rhythm.
12	40	7	Became positive	Became smaller	Aged 60. Coronary sclerosis, hypertension, auricular fibrillation.
13	189	42	Became positive	Became smaller	Aged 53. Hypertension, auricular fibrillation, complete A-V block.

*Burroughs and Wellcome powdered leaf (or its equivalent), $1\frac{1}{2}$ grains = 1 cat unit.

in 2 it disappeared entirely (cf. Fig. 4), and in one it became positive. The changes in the S-T and T complexes following digitalization are rapid and, on occasion, rather striking. In several instances, particularly in patients with heart disease, the contour in Lead IV closely resembled the contour seen following recent coronary occlusion (viz., Fig. 4). Since digitalis can produce changes resembling those seen in recent coronary occlusion, it is important to determine whether or not digitalis has been given in a particular patient before arriving

at a final diagnosis. A final evaluation may sometimes depend on comparing the records with those obtained following a subsequent digitalization.

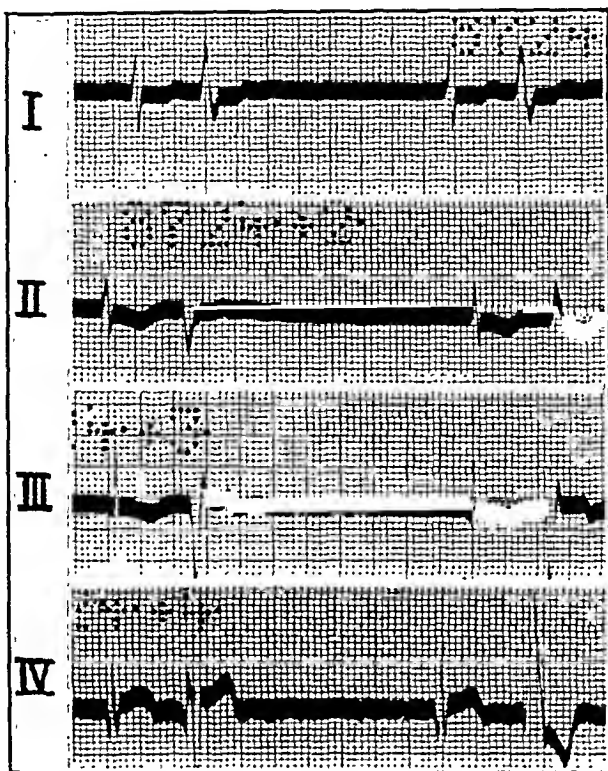


Fig. 4.—Four lead electrocardiograms taken during digitalis intoxication in Subject 9 (Table I). (Note the complete A-V block and the bigeminus with ventricular extrasystole from several foci.)

SUMMARY

Digitalis in large doses produces rapid changes in Lead IV which occasionally resemble, and consequently must not be confused with, those seen in recent coronary occlusion.

We are grateful to the volunteers who acted as subjects for this experiment. Since this communication was submitted for publication, we have seen thirteen more instances of digitalis distortion of Lead IV. In several the problem of differentiating the change from that due to a recent coronary occlusion presented considerable difficulty.

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GALLBLADDER-HEART REFLEXES IN MAN UNDER SPINAL ANESTHESIA*†

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CARDIAC irregularities in gallbladder disease are clinically important. Years ago Babcock¹ called attention to the frequency of myocardial incompetence associated with chronic cholecystitis, which was alleviated following operative relief of the gallbladder condition. He offered as the most likely explanation a reflex action resulting from irritation of the splanchnic and pneumogastric filaments distributed to the wall of the gallbladder.

Osler² pointed out that patients with biliary colic may die of cardiac standstill. Mayo³ and others have observed cardiac arrhythmias associated with biliary tract disease. Straus and Hamburger⁴ reported 4 cases of diseased gallbladders associated with definite cardiac irregularities, shown either by electrocardiograph or pulse. In 3 of the cases the irregularities disappeared postoperatively. Buchbinder⁵ demonstrated that the sudden release of bile from an incised frog's gallbladder was attended by transient arrest followed by sinus bradycardia. He concluded that a specific reflex to the heart, of vagal origin, is initiated from the gallbladder, and this is perhaps the basis for the arrhythmias in man with gallbladder disease. With reference to the reflexogenic nature of this phenomenon, Allen⁶ showed that the pathway of impulses causing pulsus bigeminus in rabbits after insufflation of benzol came from the vicinity of the hypothalamus and the superior colliculus. Brow, Long and Beattie⁷ produced extrasystoles and tachycardias, which disappeared after experimental removal of the stellate ganglion and severance of the portion of the brain which lies between the caudal end of the optic chiasm and the cephalic end of the superior colliculus. Recently Scott and Ivy⁸ confirmed the work of Carlson and Luckhardt⁹ and the Buchbinder phenomenon, but concluded that the latter was due to the irritant action of bile on the peritoneum. They noted no change under manipulation of the gallbladder, although the mechanical stimulation of other viscera caused cardiac inhibition. Schrager and Ivy¹⁰ consider that the functional status of the cardiovascular system is the determining factor in the reaction from distention of the biliary passages. Crittenden¹¹ recently showed that cardiac arrest, heart-block, and slowing follow vomiting

*Aided by the Emil and Fanny Wedeles Fund of the Michael Reese Hospital for the Study of Diseases of the Heart and Circulation.

†From the Heart Station and the Gall Bladder Group, Michael Reese Hospital, Chicago.

induced by apomorphine; also that the heart rate in normal students increased after swallowing of stomach tubes.

The application of these experimental methods to man is not mentioned in an extensive review of the pertinent literature except for a recent report by Maher and his associates.¹² The reaction of the heart to surgical manipulations of the abdominal organs, particularly the gallbladder, is a matter of importance to the internist and the surgeon. The present report deals with the electrocardiographic manifestations during cholecystectomy under spinal anesthesia.

METHOD

The study includes a consecutive series of 17 patients with clinically proved gallbladder disease, who were subjected to operation for removal of the gallbladder. Two of the patients presented clinical evidence of slight myocardial impairment due to rheumatic or to arteriosclerotic heart disease. None of these cases was known to present any clinical evidence of cardiac arrhythmia.

TABLE I
HEART RATE CHANGES DURING GALLBLADDER MANIPULATIONS*

NO. TRIALS	PROCEDURE	ACCELERATION		SLOWING		NO EFFECT NO. CASES
		NO. CASES	CHANGE IN RATE PER MIN.	NO. CASES	CHANGE IN RATE PER MIN.	
16	Anesthesia	11	6-84	4	13-27	1
12	Pressure on gallbladder	4	7-12	2	12-15	6
11	Clamping and pulling on gallbladder	6	6-38	2	11-43	3
3	Release of gallbladder tension	1	21	2	8-11	0
12	Occlusion of cystic duct	2	8-34	6	7-41	4
10	Removal of gallbladder	4	13- 2	4	13-24	2
8	Pressure on right kidney	2	9-20	3	16-56	3

*Changes of less than 6 beats per minute were considered within the limits of experimental error.

Spinal anesthesia was used in all cases. The spinal anesthetic employed was either spinocain or nupercain, in the dosage of about 250 mg. properly injected at the level of the first or second lumbar interspaces. Effective anesthesia was obtained as high as the level of the first thoracic, and was tested by means of a sharp instrument applied to the operative field fifteen to twenty-five minutes after the administration of the drug.

The usual arrangement to take electrocardiograms was made, care being observed to avoid the operative field. The electrocardiograms were recorded on a mobile machine brought directly into the operating room. Records were taken before and after effective anesthesia and during the various steps of the usual cholecystectomy, with control readings before and after each step whenever possible. It was not always feasible to obtain control records because of the danger to the patient of prolonging the operation.

The electrocardiographic records were studied with respect to (A) rate changes, (B) arrhythmias or ectopic beats.

A. Rate changes are presented in Table I. The results are variable, but the usual effects of anesthesia, pressure, clamping and pulling on the gallbladder were to increase the heart rate over control periods. On the other hand, both the release of gallbladder tension and the occlusion of the cystic duct usually caused inhibition of the heart. The effect of pressure on the kidney was variable.

B. Arrhythmias or ectopic beats. In the entire series, 3 patients developed cardiac irregularities during the operation; 2, ectopic beats; and 1, sinus arrhythmia. One patient, in whom ectopic beats were present, showed an increase in their frequency during the operation. Two of the patients developed ventricular extrasystoles, one during the ligation and cutting of the cystic duct and artery, the other during the period of pressure on the gallbladder. Two patients showed ectopic beats of nodal origin, in one during the initial control record and in the other only during the period of tested effective anesthesia. The former patient had ventricular extrasystoles during the period of tested effective anesthesia and pressure on the gallbladder; in the latter sinus arrhythmia was evident after the anesthesia became effective.

SUMMARY

Sixteen cases of proved gallbladder disease were studied during cholecystectomy under spinal anesthesia by consecutive series of electrocardiograms during the usual stages of the operation. The usual effects of pressure, clamping, and pulling on the gallbladder were to increase the heart rate. Only two of the sixteen patients developed ectopic beats during operation. One having such ectopic beats before operation showed an increase in their frequency during operation. One instance of sinus arrhythmia developed during the operation. These changes are taken to indicate reflex effects on the heart from the operative field.

We wish to express our thanks to Dr. L. N. Katz for his guidance and criticism.

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Department of Clinical Reports

A CASE OF SINO-AURICULAR BLOCK AND ALMOST COMPLETE A-V DISSOCIATION WITHOUT PRIMARY A-V BLOCK*†

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AN UNUSUAL type of cardiac arrhythmia is reported because of the rarity of its occurrence and the difficulty of its interpretation. The interpretation was arrived at after the records were analyzed according to the method developed by Zeisler in this laboratory.¹

The records of this patient are shown in Fig. 1. The P-P intervals are given in the top lines and the R-R intervals in the bottom lines above each record. The oblique lines represent the R-P and P-R intervals. Conducted beats are shown by heavy oblique lines with arrows. In Leads II, III, and IV there is overlapping where long strips had to be cut for illustration.

In attempting to unravel the mechanism attention was first paid to the P-P intervals; it was soon evident that the P-P intervals fell into 4 groups (see Table I), having a least common denominator (a value in the neighborhood of 0.57 sec.). This indicates that this is a case of S-A block, the ratio of conducted sinus beats varying from 1:1 to 4:1. The variations in the P-P intervals in each group are due to the presence of a moderate sinus arrhythmia with shifting pacemaker as shown by the variation in contour of the P-wave, especially seen in Leads III and IV (Fig. 1).

The long pauses between sinus beats permit frequent nodal escape-ment. The intervals before the A-V node discharged vary considerably, indicating that this node also has an arrhythmic discharge. This is not usual in nodal escape. The P-wave following the nodal escape often reached the A-V node and bundle during its refractory period (interference dissociation). When the P-wave reached the A-V junctional tissue a little later, it was conducted through usually with a normal but occasionally with a prolonged P-R interval (see Table II). Twice this prolonged P-R interval (0.24 second) was present with a relatively long preceding R-P interval (0.84 and 0.78 sec.). It may

*From the Heart Station, Michael Reese Hospital, Chicago.

†Aided by the Frederick K. Babson Fund for Diseases of the Heart and Circulation.

TABLE I

P-P INTERVALS ASSEMBLED ACCORDING TO VIEW AS TO MANNER OF S-A CONDUCTION

	1:1 SEC.	2:1 SEC.	3:1 SEC.	4:1 SEC.
	0.60	1.32	1.52	2.24
	0.68	1.20	1.50	2.20
	0.44	1.28	1.48	2.26
	0.70	1.14	1.62	2.24
	0.50	1.34		2.26
	0.56	1.24	1.54	2.22
	0.48		1.42	2.24
	0.54			2.06
	0.58			2.32
	0.56			1.92
	0.56			2.38
	0.60			2.26
				2.24
				2.28
				2.18
				2.12
				2.30
				2.18
				2.20
				2.04
Average P-P Interval	0.57	$125 =$ 0.62×2	$1.51 =$ 0.54×3	$220 =$ 0.55×4
Variation	0.44 - 0.70	$1.14 - 1.34 =$ $(0.57 - 0.67) \times 2$	$1.42 - 1.62 =$ $(0.47 - 0.64) \times 3$	$192 - 238 =$ $(0.48 - 0.60) \times 4$

TABLE II

RELATION OF P-R TO R-P INTERVAL, ARRANGED ACCORDING TO R-P INTERVAL DURATION

R-P INTERVAL SEC.	P-R INTERVAL SEC.	R-P INTERVAL SEC.	P-R INTERVAL SEC.
1.68	0.16	0.44	0.20
1.36	0.16	0.44	0.20
1.36	0.14	0.36	0.22
1.30	0.18	0.36	—*
1.28	0.18	0.34	0.36
1.26	0.16	0.34	—
1.22	0.14	0.30	0.42
1.18	0.20	0.26	0.44
1.12	0.16	0.24	—
1.12	0.20	0.22	0.20 P ₄ -R ₅ (IV)
1.08	0.16	0.20	—
1.04	0.20	0.20	—
0.94	0.16	0.20	—
0.88	0.20	0.20	—
0.88	0.20	0.18	—
0.88	0.14	0.16	—
0.84	0.24 P ₉ -R ₈ (III)	0.16	—
0.80	0.16	0.12	—
0.78	0.24 P ₁₃ -R ₁₂ (III)	0.08	—
0.76	0.20	0.08	—
0.72	0.18	0.04	—
0.70	0.20	0.00	0.44 P ₆ -R ₅ (II)
		-0.08	—

*Blocked out.

instances of a supranormal phase but are in all probability due to the improvement of the nourishment of the junctional A-V tissues shortening the refractory period.

Aberrant conduction was found when a ventricular beat occurred soon after its predecessor, viz., R₉ Lead II, R₄, R₅ and R₁₂ Lead IV, when it might be expected that the impulses would reach the conduction system of the ventricles during their relative refractory phase.

SUMMARY

An unusual case of cardiac arrhythmia is presented which shows sino-auricular block of varying degrees, 2:1, 3:1 and 4:1, almost complete A-V dissociation without primary A-V block, nodal escapement, aberrant conduction, and sinus arrhythmia with shifting pacemaker.

This case illustrates the advantages of the method of analysis developed in this laboratory in aiding the interpretation of such cases.

It is a pleasure to express my indebtedness to Dr. Louis N. Katz, at whose suggestion this analysis was made, for his helpful advice and criticism. We are indebted to Dr. M. Lev, whose patient this was, for permitting us to take these electrocardiograms. A second electrocardiogram taken six months later showed similar disturbances.

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Department of Reviews and Abstracts

Selected Abstracts

Schneider, Edward C., and Crampton, C. B.: The Effect of Posture on the Minute Volume of the Heart. *Am. J. Physiol.* 110: 14, 1934.

Using the Grollman acetylene method, the minute volume of the heart has been studied on seven healthy male subjects to determine the effect postural change in the body may have on the heart output. From this study the authors conclude that the minute volume of the heart is increased in the recumbent as compared with the erect position.

Ordinarily on prolonged quiet standing the output of the heart either remains unchanged or decreases slightly in subjects displaying no distress as a result of the long standing. The heart output is decreased in subjects who on long quiet standing display poor circulatory compensation in the erect position. A pulse pressure below 20 mm. of mercury indicates a falling cardiac output.

Lisa, James R., and Chandlee, Gertrude Jackson: The Heart and Great Vessels in Combined Syphilitic and Rheumatic Infection. *Arch. Int. Med.* 54: 952, 1934.

The lesions and the clinical course in six cases of combined syphilitic and rheumatic infection of the heart and great vessels were mainly rheumatic. In one case only was the rôle of syphilis of equal importance to that of rheumatic infection. The combined active infections carry a much graver prognosis than either infection occurring separately. Heart sounds help in the differential diagnosis of rheumatic and syphilitic aortic disease. Roentgenology is a valuable aid in the differential diagnosis between the rôles of syphilis and rheumatic infection in the production of cardiovascular pathologic processes. Syphilis of the myocardium could not be proved in any of the cases.

Graybiel, Ashton, Allen, Arthur W., and White, Paul D.: A Histological Study of the Arterioles of the Muscle and Skin From the Arm and Leg in Individuals With Coarctation of the Aorta. *J. Clin. Investigation* 14: 52, 1935.

It was found that the hypertension associated with coarctation of the aorta in five young individuals did not cause sclerosis of the arterioles or smallest arteries of the skin or voluntary muscles. In the five cases, the systolic blood pressure in the arm averaged 70 mm. more than that in the leg and the diastolic pressure in the arm 28 mm. more than that in the leg. Nevertheless, it was impossible by biopsy in these cases to distinguish the arterioles and smallest arteries of the arm from those of the leg.

Bishop, Paul A., and Roesler, Hugo: The Roentgenologic Diagnosis of Intracardiac Calcifications. *Am. J. Roentgenol.* 31: 1, 1934.

The frequency of postmortem findings of calcification of the left-sided annuli fibrosi and the aortic and mitral valves is cited. Attention is called to the few reports of the roentgen observation of these calcifications in the living and the

rarity of correct diagnosis of their location. Three such cases are reported, all of them confirmed by autopsy study. The characteristic features of appearance, location, and motion of these shadows in roentgenoscopic study are described, together with points of differential diagnosis. The technic for making films to show the calcification is described.

It is the authors' belief that these calcifications are more frequent than is realized and that the roentgenologist can play the leading rôle in their recognition by routine roentgenoscopic observation of the heart in routine chest examinations. Some physiologico-pathological aspects of this type of calcareous degeneration are described, together with illustrative cases from the literature.

Scupham, George W.: Effect of Theobromine on Peripheral Vascular Disease. Arch. Int. Med. 54: 685, 1934.

Theobromine and its salts, particularly theobromine sodium acetate, act as peripheral vasodilators and are useful in the treatment of peripheral arteriosclerosis and early cases of thromboangiitis obliterans in which there is a large element of angiospasm. Their use results in subjective improvement in intermittent claudication, and repair of loss of tissue integrity has been noted. These drugs are not effective in all cases, but the results obtained with them are sufficiently good to make them a valuable adjunct in the treatment of peripheral vascular diseases.

Nahum, L. H., and Hoff, H. E.: The Effect of Injection of Monoiodoacetic Acid and Sodium Cyanide on the Mammalian Heart. Am. J. Physiol. 110: 56, 1934.

Experiments were undertaken to study the effect on the electrocardiogram of poisoning with monoiodoacetic acid, which prevents the accumulation of lactic acid and sodium cyanide which promotes such accumulation of lactic acid.

It is believed that the failure of the anaerobic energy system of the heart induced by monoiodoacetic acid leads to an acceleration in heart rate, a decrease in conduction time, and a reduction of the duration of the ventricular complex as well as to profound alterations in the ventricular complex characterized by a change in the direction of the T-wave, disappearance of the isoelectric interval, and displacement of the S-T segment.

The suppression of oxidations by cyanide results in marked slowing of the heart rate, gradual development of A-V block and prolongation of the duration of the ventricular complex without further permanent changes in the ventricular complex.

It is concluded that the pacemaker and conducting tissue of the heart operate essentially on aerobic energy while the myocardium is primarily anaerobic. Changes in the S-T segment of the electrocardiogram in these experiments are related, not to accumulation of metabolites nor to failure of oxidations, but to a loss of the anaerobic energy of glycogen breakdown.

Page, Irvine H.: Acetyl-Beta-Methylcholin. Observations Concerning Its Action on the Blood Pressure, Skin Temperature and the Heart, as Exhibited by the Electrocardiogram of Hypertensive Patients. Am. J. M. Sc. 189: 55, 1935.

Mecholin (acetyl- β -methylcholin), administered subcutaneously, greatly increases the temperature of the skin of the face and trunk of patients suffering from arterial hypertension; the hands and feet usually remain almost unaffected. Administered by mouth it fails to have this action. Doses of 4 gm. taken by mouth have either no effect on the average blood pressure or a slight one only.

When administered subcutaneously, mecholin usually causes inversion of the T-waves of the electrocardiogram; this effect may be abolished by injecting atropine. Except for increasing the rate, no other characteristic action of mecholin on the heart, as observed in the electrocardiograph, was seen. The size of the heart may first be decreased and then be increased briefly, the increase occurring when the level of the blood pressure has fallen markedly.

Comparison of the clinical phenomena due to injection of mecholin with those observed in patients suffering from diencephalic epilepsy, or in patients in whom pituitrin or pilocarpin had been injected into the cerebral ventricles, demonstrates a striking similarity between them. It has been suggested that many of the effects of mecholin are due to stimulation of the diencephalic parasympathetic centers and possibly the premotor area of the cerebral cortex.

Mecholin causes most of the prominent corporal characters in the play of natural emotions to appear without being accompanied by the psychical counterpart itself.

Edeiken, Joseph, and Wolferth, Charles C.: Clinical Significance of the M or W Shaped Q-R-S Complex in Lead II of the Electrocardiogram. *Am. J. M. Sc.* 188: 842, 1934.

An M or W-wave in Lead II of the electrocardiogram having the characteristics defined in this paper has not been observed in tracings of 1,077 presumably normal adults. It was seen five times (4.3 per cent) in 116 patients with the anginal syndrome. After a period of three years, four of the five patients are dead, the other incapacitated.

In 4,450 unselected electrocardiograms of hospital and clinic patients, the M or W-wave was seen in 21 tracings (0.47 per cent). Of these patients 14 are dead and six show clinical evidence of severe myocardial disease; one cannot be traced. The electrocardiograms of two of the six patients who are alive show bundle-branch block, one complete A-V dissociation, and the other three have had a coronary occlusion and are more or less incapacitated. Only two of this group have lived more than three years after the M or W-wave was first observed, and both of these are incapacitated because of pain on effort.

Of twenty-five isolated cases observed during the past two years, twenty (80 per cent) were from patients with coronary occlusion. Nine of the patients are dead; thirteen of the remainder are from the groups suspected of having had a coronary occlusion, one suffered from hypertension, and the two remaining cases are obscure and in one of these no other evidence of cardiovascular disease was found.

In most cases, the M or W-wave is probably due to an intraventricular conduction abnormality as a result of myocardial disease. Pathological changes were widespread in the three cases in which necropsy was obtained. It is possible, however, that a congenital anomaly of conduction may occasionally produce complexes of this type.

In some cases, the M or W complex has been present throughout the entire period of observation. In others, it has been relatively transient. Its appearance time following coronary occlusion is variable, the range observed in serial electrocardiograms being one day to three months.

Veal, J. Ross, and McFetridge, Elizabeth M.: Adequate Circulation in the Extremities. Arteriography as a Test for Determining Its Limits. *J. A. M. A.* 104: 542, 1935.

Thirty consecutive cases of gangrene of the extremities as a result of peripheral vascular disease have been studied by means of arteriography before amputation.

It is believed that arteriography is a very much more reliable index of the limits of adequate circulation than is either the histamine reaction or the salt solution test. It is believed that the use of this test in conjunction with proper preoperative and postoperative therapy will furnish one more safeguard for the patient with gangrene of the extremities.

Allen, Edgar V., and Camp, John D.: Arteriography. J. A. M. A. 104: 618, 1935.

In the opinion of the authors, the chief value of arteriography lies not in the direction of diagnosis but in that of pathogenesis. It gives information of inestimable value regarding the minutiae of arterial disease, information which can be secured in no other way. It is to be expected that the absence or presence of organic arterial change in Raynaud's disease and the part played by disturbances in arterial circulation in scleroderma can be determined. In thromboangiitis obliterans, the part played by collateral arteries and other adjustments to impaired circulation are portrayed in a manner that leaves little to be desired. The mode of progression of the disease and the compensation for it are clearly outlined. The situation, extent, and nature of aneurysms, arteriovenous fistulas and arterial emboli can be determined accurately by arteriography.

Proger, S. H., and Korth, C.: Effect of Light Muscular Training on Patients With Heart Disease. Arch. Int. Med. 55: 204, 1935.

Six patients with rheumatic heart disease pedaled on a stationary bicycle for from one to two hours daily for a period of from five to six weeks. Two normal persons in the same age group served as controls. There were essentially no changes at rest in the pulse rate, respiratory rate (except for slowing in one case), pulmonary ventilation, and oxygen consumption.

In one patient in whom exercise had to be discontinued because of the development of hemoptysis, the arteriovenous oxygen difference at rest showed an increase, and the cardiac output a decrease, just before and after the hemoptysis. These values returned to normal within a few days after the exercise was discontinued. In the other patients the arteriovenous oxygen difference and cardiac output at rest were unchanged.

In the patients who improved with exercise, there was a slight slowing of the velocity of blood flow at rest. The vital capacity in two of the patients who improved with exercise showed a definite increase. In the normal subjects, as well as in the other patients, it remained unchanged. Breath-holding ability generally paralleled the vital capacity.

Of the three patients who showed definite improvement in their response to exercise, there was an increase in the height of P_2 in the electrocardiogram in one, and in the others an increase in the height of the T-waves. In the patients in whom hemoptysis developed, there was a slight prolongation of the P-R interval, an increase in the height of P_2 , and an inversion of P_3 .

There were no definite changes in the teleroentgenograms.

According to observations during exercise, the two normal subjects showed slight improvement; three patients with disease of both aortic and mitral valves showed marked improvement; one patient with only mitral disease showed no change, while another grew worse; and the only patient with an irregular heartbeat (auricular fibrillation) who also had mitral stenosis and insufficiency showed a very slight improvement.

A possible explanation for the varying responses is suggested.

In one patient, after improvement had taken place, an unexplained relapse occurred, which was overcome in a few days. In the same patient a mild infection with fever caused no change in his response to exercise immediately before and after the febrile state.

A striking parallelism is shown to exist between the pulse rate and oxygen consumption during exercise through the period of training.

Landis, Eugene M., and Hitzrot, Lewis H.: The Clinical Value of Alternate Suction and Pressure in the Treatment of Advanced Peripheral Vascular Disease. *Am. J. M. Sc.* 189: 305, 1935.

The extremities of twenty-nine patients suffering from advanced peripheral vascular disease were exposed to alternate suction (-80 to -120 mm. Hg) and pressure (+40 to +80 mm. Hg) for 25 and 5 seconds, respectively. These pressure variations were used for periods of one to two hours, at first once or twice daily, then three times weekly and finally, as symptoms diminished, once weekly. Cyanosis usually diminished; symptomatic improvement was sometimes observed, however, without significant change in skin color.

The rest pain of ischemia was usually abolished during actual use of suction and pressure and gradually became less severe in the intervals between exposure to pressure variations. Lasting relief of pain was not observed in the presence of deeply extending gangrene or large sloughs.

Ulcers, enlarging or indolent under ordinary conservative treatment, usually began to heal soon after suction and pressure therapy was instituted. Intermittent claudication became, in general, milder, and exercise tolerance was slightly, but definitely, increased.

Suction and pressure therapy was of no definite, lasting service in patients with osteomyelitis, deeply extending gangrene, or large sloughs.

This form of therapy must be applied with caution, small pressure changes being used at first. The presence of acute spreading infection or encapsulated pus must be definitely ruled out before pressure variations are used.

Suction and pressure therapy, if carefully applied, appears to be worthy of clinical trial in the treatment of peripheral vascular disease even when organic obstruction has advanced to the point where arterial blood flow can no longer be increased by vasodilatation. The method may be of service by increasing local blood flow temporarily during episodes of pain or ulceration so that time is gained for the development of adequate collateral blood flow.

Lissner, Henry H., Goffin, John L. C., and Rosenfeld, Maurice H.: The Adolescent Heart. *Am. J. Dis. Child.* 49: 353, 1935.

The study is based on observations on 2,840 children examined during a period of eight years. The diagnosis of adolescent heart was made in 254 children, or about 9 per cent. The subjective symptoms presented were the same as those usually considered as being present in patients with organic heart disease. These included palpitation, fatigue, dyspnea, pain, vertigo, sweating, cyanosis, epistaxis, and cough, occurring most frequently in the order mentioned. These are functional disturbances occurring during the period of adolescence and are probably produced by the unstable nervous system or by rapid physical development. The heart is greatly influenced during the rapid physiological changes associated with this period, and many functional disturbances are noted.

The solitary observation of an apical systolic murmur in the adolescent child is not sufficient evidence on which to base the diagnosis of organic heart disease. It

was noted that the murmur usually disappeared when the children were reexamined over a period of years. When the parents and the child were convinced that the symptoms were not due to organic heart disease, the child quickly became symptom-free; when the symptoms had been greatly impressed on the child, it was necessary to increase physical activity slowly and to overcome gradually the fear of symptoms.

During the adolescent period, the diagnosis of early organic heart disease is made too frequently on uncertain data. The differential diagnosis can be made only by the careful evaluation and analysis of all the data obtained, and in some instances a definite opinion should be given only after several years of careful observation.

Averbuck, Samuel H., and Friedman, William: Circulation Time in Normal Children. *Am. J. Dis. Child.* 49: 361, 1935.

With the use of the saccharin method, the circulation time was determined in 100 normal children ranging in age from eight to sixteen years. The technic employed is described. The average circulation time was 8.6 seconds. The range was from 5 to 13.5 seconds. In 83 of 100 tests, the limits were from 6.5 to 10 seconds. This is shorter than the circulation time in adults, determined either by the saccharin or the sodium dehydrocholate method.

The increased circulation time in children as determined by this test is due probably to two factors: first, the actual distance to be traversed from the arm to the tongue is less than that in adults; second, the execution of the test in children induces excitement and an acceleration of the heart rate.

Von Glahn, William C., and Pappenheimer, Alwin M.: Relationship Between Rheumatic and Subacute Bacterial Endocarditis. *Arch. Int. Med.* 55: 173, 1935.

Studies based on observations on a series of twenty-six consecutive cases of subacute bacterial endocarditis suggest that active rheumatic vegetations are, in persons who have had rheumatism, a necessary and practically constant prerequisite for the implantation of bacteria.

The evidence for this conclusion is summarized as follows:

1. Vegetations histologically identical with those in rheumatic endocarditis and not containing bacteria are found (a) on the same valve as the bacterial vegetations, (b) on other valves on which there are no vegetations containing bacteria, and (c) on the auricular wall.

2. Aschoff bodies in the myocardium that are taken to indicate active rheumatic disease are found in practically the same proportion of cases of subacute bacterial endocarditis as of uncomplicated rheumatic cardiac disease.

3. Types of bacterial endocarditis other than that due to nonhemolytic streptococci may be engrafted on active rheumatic vegetations. This is a cogent argument against the view that the two types of lesions are a response of different intensity to the same infective agent, unless the current views as to the histological specificity of the rheumatic reaction are dispensed with.

Faulkner, James M., Place, Edwin H., and Ohler, W. Richard: The Effect of Scarlet Fever Upon the Heart. *Am. J. M. Sc.* 189: 352, 1935.

An electrocardiographic study was made of 171 cases of scarlet fever during and following the acute infection. Abnormal electrocardiograms were noted in eleven cases. The abnormalities consisted of prolongation of the P-R interval in five cases and flattening or inversion of the T-wave in six cases and did not appear before the thirteenth day from the onset of the scarlet fever in a single instance.

A follow-up study of 600 cases of scarlet fever was made from one to three years after the acute infection. It was found that seven of these individuals had developed heart disease in the interval. The type of heart disease found was indistinguishable clinically from rheumatic heart disease.

McMahon, H. E., and Pratt, J. H.: Malignant Nephrosclerosis (Malignant Hypertension). *Am. J. M. Sc.* 189, 221, 1935.

The clinical and anatomical findings in a consecutive series of 100 patients with malignant nephrosclerosis, who came to autopsy, are described. Essential lesions occur in the blood vessels throughout the body, especially in the heart and kidneys.

The authors believe that malignant nephrosclerosis should not be looked upon as merely a progression of benign nephrosclerosis, but rather as a distinct and separate disease. It may occur alone or as a terminal complication of the benign disease. In the very early stages, when only the cardiovascular signs and symptoms are present, it may be impossible not only to say whether one is dealing with an early case of benign or malignant nephrosclerosis, but also it may be equally impossible to predict into which of these diseases the case will ultimately fall. As the disease progresses, the renal component becomes more and more conspicuous, and in the late stages it may be impossible to differentiate this disease from chronic glomerulonephritis. The etiology of benign and malignant nephrosclerosis has probably much in common, for one sees cases of chronic lead poisoning, pituitary basophilism, toxemias of pregnancy, and so on, which on the one hand may show benign nephrosclerosis and on the other, the much less frequent malignant disease. The course and prognosis depend not alone on the quality and quantity of the exciting agent but also in the manner in which the vessel wall responds. If the response is of a simple degenerative nature, the disease progresses slowly, the prognosis is good, and such cases are classed as benign nephrosclerosis. If the vascular response is characterized by inflammatory changes of the intima, necrosis, and hemorrhage, the course is more rapid, the prognosis is poor, and such cases are classed as malignant nephrosclerosis.

Brown, Samuel, and Alexander, Benjamin: Duroziez's Sign in Normal Subjects and in Patients With Arterial Hypertension With Special Reference to Its Relation to Capillary Pulsation and the Forward Flow of Blood During Diastole. *J. Clin. Investigation* 14: 285, 1935.

The purpose of this investigation was to study in health and vascular disease the incidence of Duroziez's sign artificially produced by immersing the arm in water at 114° F.; to correlate this sign with other peripheral vascular signs such as capillary pulsation, blood pressure, and pulse pressure; to evaluate Duroziez's sign as an index of the dilatability of the peripheral vascular bed.

In sixty-three subjects with no evidence of cardiovascular disease, the incidence of Duroziez's sign decreased with advancing years. This indicates a progressive inability of the peripheral minute vessels to dilate sufficiently as age advances to provide the increased diastolic forward flow of blood necessary to produce the sign.

The incidence of the sign was studied in forty-one subjects with clinical hypertension. Compared to normal subjects of similar age groups, the incidence was in general lower, particularly with advancing age. This is in accord with the theory that arteriosclerosis is associated with arterial hypertension.

Subjects with wide pulse pressures generally showed a low incidence of Duroziez's sign of the peripheral type. This probably is due to the general coexistence of arterial and arteriosclerosis.

Capillary pulsation was studied both immediately before and after immersion of the arm in water at 114° F. Of sixty-one subjects with no evidence of vascular disease, 31 per cent exhibited it spontaneously. Of forty-one subjects with clinical hypertension, 54 per cent showed a spontaneous capillary pulsation. There was no apparent relation to age.

Capillary pulsation was particularly evident in subjects with wide pulse pressures. The greater incidence of spontaneous capillary pulsation in the hypertensive group was probably due to the greater pulse pressure generally seen in this disease.

The height of diastolic blood pressure seemed in no way to influence the incidence of spontaneous capillary pulsation except so far as the height of diastolic pressure affected the magnitude of pulse pressure.

Capillary pulsation after immersion at 114° F. was present in every case. The ages of the subjects ranged from twenty to seventy-three years. Capillary pulsation, since it was always present in the heated skin, regardless of age, cannot be used as a qualitative test of the condition of the peripheral arterioles.

Duroziez's sign produced in the manner described may be used to throw light on the general condition of the peripheral arterioles. According to these findings, any person under the age of thirty-five who fails to show a Duroziez's sign after immersion of the arm in water at 114° F. digresses from the physiological norm in that his functional peripheral vascular bed is relatively fixed.

Bierring, Walter L., Bone, H. C., and Lockhart, M. L.: Use of the Electrostethograph for Recording Heart Sounds. *J. A. M. A.* 104: 628, 1935.

The electrostethograph was designed and built by one of the authors. The principle of construction is described briefly in the article. Records of heart sounds are reproduced, illustrating the various auditory phenomena which may be heard, both murmurs and changes in sounds. The instrument offers a satisfactory method of photographing heart sounds and appears to have certain advantages over other types of recording devices. The photographic record of heart sounds is of distinct aid as a supplement to auscultatory observation as well as providing a permanent graphic record.

McEwen, Currier: Cytologic Studies on Rheumatic Fever. II. Cells of Rheumatic Exudates. *J. Clin. Investigation* 14: 190, 1935.

The amount, character, and cellular content of exudates from patients with rheumatic fever were studied in relation to certain clinical aspects of the disease and were compared with those of nonrheumatic exudates.

There was no obvious correlation between the amount of synovial fluid and the severity of arthritis; the number of cells per cubic millimeter ranged between 800 and 47,000, and the total number contained in the exudates tended to vary directly with the stage and severity of arthritis; the differential formula appeared to bear some direct relationship to the stage of arthritis and the age of the patient. Supravital stains revealed no cells similar to those previously described in rheumatic granulomas. Early there was a predominance of polymorphonuclear neutrophils, with a few monocytes and undifferentiated young connective tissue cells; later there were numerous clasmotocytes containing debris and degenerating cells. Rheumatic pleural and pericardial exudates contained cells similar to those of the joints but with the addition of a few mesothelial elements. Because nonrheumatic exudates were similar in microscopical content, no specific character could be assigned to exudates in rheumatic fever.

Hitzig, William M., King, Frederick H., and Fishberg, Arthur M.: *Circulation Time in Failure of the Left Side of the Heart*. Arch. Int. Med. 55: 112, 1935.

In isolated failure of the left side of the heart, the arm-to-tongue circulation time is almost always prolonged, sometimes to three times the normal value. This circulation time was measured by the injection of gluside described by the authors. On the other hand, the arm-to-lung circulation time measured by a method described by one of the authors may be normal in failure of the left side of the heart despite markedly prolonged arm-to-tongue circulation time. This shows that the prolongation of the arm-to-tongue circulation time in these cases is due to slowing of the pulmonary blood flow down stream to the arterial capillaries of the lung. The prolongation of the arm-to-tongue circulation time does not always parallel the severity of the other symptoms of failure of the left side of the heart. In exceptional cases, the arm-to-tongue circulation time is within normal limits despite severe symptoms of failure of the left side of the heart.

The circulation time in failure of the left side of the heart with normal rhythm may be shortened by digitalization, furnishing further objective evidence of the utility of digitalis in many patients with this circulation disturbance. The systemic venous pressure is normal in isolated failure of the left side of the heart.

Nuzum, Franklin R., and Elliot, Albert H.: *Transverse Diameter of the Heart in Patients With Hypertension, With Clinical Measurements Checked by Post-mortem Studies*. Arch. Int. Med. 55: 293, 1935.

The ratio of the transverse cardiac diameter to the internal diameter of the chest (Danzon ratio), as determined by orthodiagraphy, was compared with the predicted normal cardiac diameters of Hodges and Eyster in 175 persons without heart disease previously reported on and in 79 persons with arterial hypertension.

A direct correlation was found between the cardiothoracic ratio and the body weight in persons both with and without potential cardiac enlargement, such that thin persons tended to have transverse cardiac diameters less than one-half the internal diameter of the chest and obese persons had cardiac diameters greater than this by more than the experimental error of the determination.

The predicted diameters of Hodges and Eyster, while approaching more closely the actual diameters found in persons without cardiac enlargement, failed to disclose the presence of left ventricular enlargement in obese persons, but were a satisfactory guide in normal or underweight subjects. It is suggested that this is not the fault of the standard per se, but is due to the failure of left ventricular enlargement, through mechanical causes, to manifest itself by a detectable increase in the transverse diameter of the heart in obesity.

Both methods failed to demonstrate enlargement in 20.2 per cent ± 8.5 of seventy-nine persons who presumably had cardiac hypertrophy.

A comparison of the incidence of cardiac enlargement, as defined by these standards, with the occurrence of left axis deviation in the electrocardiogram showed that the correlation is too indefinite to be of value in judging the relative efficacy of such measurements proposed for the detection of cardiac enlargement.

Book Reviews

KLINIK DER ERKRAUKUNGEN DES HERZMUSKELS. X FORTBILDUNG-LEHRGANG IN BAD-NAUHEIM. September 20-23, 1934. Edited by the Union of Bad-Nauheim Physicians. Theodor Steinkopff, Dresden and Leipzig, 1934.

This volume of 170 pages includes 16 lectures delivered in the annual Extension Course to Physicians given at Bad-Nauheim in the subject of cardiovascular diseases. The topic chosen for the present course is that relating to various aspects of the myocardium and its diseases. The contributions have been made by well-known students of the subjects and merit careful consideration and study.

L. A. C.

ILLUSTRATIVE ELECTROCARDIOGRAPHY. By the late Joseph H. Bainton, M.D., Attending Physician and Chief of the Cardiac Clinic, Morrisania City Hospital, and by Julius Burstein, M.D., Associate Electrocardiographer, Morrisania City Hospital, New York, N. Y. 258 pages, 100 plates. The D. Appleton-Century Co., New York and London, 1935.

The authors state that this book was planned specifically for the general practitioner. The text, for the most part, consists of legends for the illustrations. Each new subject, however, is introduced by a brief explanatory discussion to orient the uninitiated reader and prepare him to study the illustrations. The 155 electrocardiograms presented in the 100 plates have been clearly marked and arranged "in a graded sequence from normal to abnormal and from simple to more complicated phenomena." Nearly all the illustrations have been judiciously selected.

This book, in the opinion of the reviewer, offers to the general practitioner and to the casual practitioner of electrocardiography, the least painful approach to the subject thus far available. The proportion between text and illustrations is such as to avoid discouraging the not too enthusiastic seeker after knowledge, who nevertheless wishes to know something about electrocardiography. If he studies each illustration until he understands it and learns to recognize the significant features without referring to the text (not a difficult procedure and at least as interesting as solitaire), he cannot fail to emerge with a reasonable knowledge of the subject. This book is the one to be recommended to those who ask what they should read to learn something about electrocardiography.

C. C. W.

LES NÉVROSES TACHYCARDIQUES. By Dr. L. Gallavardin and Dr. A. Tourniaire. Masson & Cie., Paris, 1935, 122 pages with 24 illustrations.

In this monograph Dr. Gallavardin and Dr. Tourniaire discuss the condition known as irritable heart, effort syndrome, or neurocirculatory asthenia, which they consider to have as its most outstanding feature an instable, rapid heart rate. They point out that although the symptoms are cardiac, the heart is essentially normal and signs of cardiac failure never appear, and they repeat that the fundamental trouble is a constitutional hyperexcitability of the sympathetic nervous system. They stress the uselessness of drugs and the importance of graded exercise and reeducation in the treatment of this condition. In addition to their own observations and impressions, the authors present a survey of the literature and an extensive bibliography.

E. H.

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